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PRESENT STATUS OF CARDIOVASCULAR SURGERY

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This review is designed to outline the present status of surgery for cardiovascular disease with particular attention to more recent advances in the field. It is not proposed to review all of the advances of the past 10 to 15 years, since this would carry us beyond the scope of this review and since much of the information concerning the fundamental work has been widely distributed. The diagnostic aspects will be neglected except in instances in which recent developments have radically altered our concept of the disease. The basic surgical treatment of well-established entities will be referred to only briefly as a background for evaluation of more recent advances in this field.

No clear-cut division will be made between clinical and experimental approaches to the problem, since the transition from the development of the procedure in the experimental laboratory to clinical application in the hospital operating room is now extremely rapid. Attention will be confined to treatment of lesions in the heart and its immediately adjacent great blood vessels, and no consideration will be given to peripheral vascular disease, to aortic aneurysms, or to certain other anomalies of little importance at present. The method of surgical treatment will be discussed according to whether the lesion is acquired or congenital.

Congenital anomalies that may require surgical intervention include (1) patent ductus arteriosus, (2) coarctation of the aorta, (3) aortic rings and other vascular anomalies, (4) septal defects, and (5) cyanotic heart disease. The last category may include conditions such as (*a*) the tetralogy of Fallot, (*b*) pure pulmonary stenosis, and (*c*) transposition of great vessels, as well as (*d*) other anomalies.

Acquired cardiovascular conditions that may necessitate operative intervention include (1) tumors of the heart, (2) foreign bodies in the heart, (3) wounds of the heart, (4) suppurative pericarditis, (5) constrictive pericarditis, (6) coronary insufficiency, and (7) valvular lesions such as (*a*) mitral stenosis and (*b*) aortic stenosis.

CONGENITAL LESIONS

Patent Ductus Arteriosus.—Since the first successful ligation of a patent ductus arteriosus by Gross, in 1938, there have been thousands of operations for this condition. The diagnosis has been generally considered an extremely simple matter, with chief reliance on auscultatory findings. In the absence of a typical machinery murmur the diagnosis has rarely been made, and most authorities have felt that surgery in such patients is not indicated. Recently, however, Dammann has reported some 15 instances in which the classical auscultatory findings of patent ductus arteriosus were absent but the diagnosis was strongly considered on other clinical grounds and was confirmed by cardiac catheterization and by operation. In each instance, the ductus was large and pulmonary hypertension was present. It is felt that the pulmonary hypertension accounted for the absence of a continuous murmur.

The diagnosis of patent ductus arteriosus in infants without classical manifestations of this condition has also been reported by Keith and Forsyth. They determined the presence of this abnormality by iodopyracet aortography in four infants with serious heart failure. It is to be hoped that further refinement of diagnostic techniques will permit surgical therapy in even more instances of patent ductus arteriosus, treatment of which is attended by such gratifying results. In an uncomplicated case, an operative mortality rate of about 1% may reasonably be expected. On this basis, there is little reason to withhold operation and thereby expose the patient to the risk of physical maldevelopment, cardiac failure, or subacute bacterial endocarditis. Although the interruption of a patent ductus arteriosus in the presence of superimposed bacterial infection may be curative even without antibiotic therapy, it is customary to employ massive, long-continued doses of antibacterial agents, of which at least a short course is given before operation. There is increased morbidity and mortality in patients with such complicated conditions as well as in patients of the older age group. For this reason, surgery should be advised in almost every instance when the diagnosis is made. The

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optimal time is not agreed on, but it no longer seems advisable to delay surgery merely to "let the child get bigger." The initial technique of simple ligation of the ductus has now been supplanted by either multiple suture-ligation or by complete division. While both of these techniques have been reported to give excellent results with a very low recurrence rate, the operation of complete division seems theoretically less likely to be followed by recurrence.

An unusual congenital malformation that produces a clinical picture similar to patent ductus arteriosus is an aortic septal defect, with an opening between the aorta and the pulmonary conus just above the valves. Cardiac catheterization or angiography may occasionally distinguish between this lesion and patent ductus arteriosus. The diagnosis is clear at operation, but surgical correction is a formidable procedure that has been attempted successfully on rare occasions.

Coarctation of the Aorta.—This not uncommon abnormality is generally divided into "infantile" and "adult" types, depending on the site and character of the aortic narrowing. There is good reason to discard these categories and replace them with descriptive terms, such as "diffuse" or "localized." The usual sharply localized narrowing just beyond the origin of the left subclavian artery may be treated successfully by resection of the narrowed segment and end to end anastomosis of the aorta. More diffuse areas of coarctation may necessitate the use of the left subclavian artery, which is the vessel originally employed in the 1943 experiments of Blalock and Park. This gives satisfactory results if the vessel is not twisted in rotating it downward. A third alternative, employed with success by Gross and others, is the use of preserved aortic grafts from suitable autopsy material. A number of these grafts are functioning satisfactorily in their second year.

Although the diagnosis of coarctation is usually made simply on the basis of the presence of hypertension in the upper extremities and hypotension below, there are a number of instances in which angiography may be of value. It may localize coarctation at unusual sites, differentiate a localized from a diffuse coarctation, or detect the presence of aneurysm near the coarctate segment. The combined use of cardiac catheterization and angiography may add somewhat to the reliability of the diagnosis, but it also carries with it the morbidity and possible mortality of both procedures. Hence the combined procedure is not recommended for routine employment in the study of coarctation. The use of tomography may give such precise information on the site and character of the coarctation that angiography may not infrequently be omitted.

While we are still ignorant of the cause of coarctation, it has been produced experimentally and a variety of studies have been directed toward explaining the nature of the resultant hypertension. In a series of ingenious experiments, Scott and Bahnson have produced coarctation in dogs by the method of Blalock and Park and have observed subsidence of the resultant hypertension after unilateral nephrectomy and transplantation of the remaining kidney to the neck. This is strong evidence in favor of a renal factor in the hypertension of aortic coarctation. When the remaining kidney was transplanted to the groin, the hypertension persisted for four and one-half months in one instance. Further studies are being conducted to clarify these observations.

The present status of the operative attack on coarctation is typified by the first 100 cases reported by Gross. In this series, there were 11 deaths in the immediate postoperative period and nine patients in whom only exploration was performed. Of the 80 patients in whom a definitive procedure was possible, 71 were considered to be cured, with partial relief in 8 and no improvement in 1. With increasing experience and more operations in the earlier age group, future results should show improvement.

There has been much discussion as to the optimal time for operation in coarctation of the aorta. Obviously, the earlier the condition can be corrected, the less will be the likelihood of related complications. On the other hand, if coarctation is corrected at such an early age that failure of the anastomosis to grow would establish a relative coarctation at a later date, there would be cause for delaying the procedure. Research on the growth of vascular anastomoses has demonstrated a number of suturing techniques with which one may anticipate satisfactory increase in the size of the anastomosis comparable with the increase in size of the adjacent vessels. This is possible with both absorbable and nonabsorbable suture material. Therefore, it seems that the small size of the aorta per se offers no contraindication to resection of a coarctation and end to end anastomosis.

Aortic Rings and Other Vascular Anomalies.—The frequent occurrence of vascular anomalies within the chest has been commented on for many years, but it was not until 1933 that Sprague and others suggested the possibility of surgical intervention for relief of symptoms from such anomalies. Such surgery was first successfully carried out by Gross, in 1945, to relieve tracheal obstruction by a vascular ring.

The classification and treatment of aortic rings and other vascular anomalies that compress the trachea and esophagus has been published by Gross and Neuhauser, on the basis of 40 patients treated surgically. A double aortic arch generally presents symptoms of respiratory obstruction in infants below the age of six months. These symptoms are strikingly relieved by division of the smaller arch. When a right aortic arch is associated with a left ligamentum arteriosum, similar symptoms may be produced, although generally at a later age. The brachiocephalic trunks may arise from the aorta in a variety of ways to produce compression of the trachea or esophagus. If this compression causes symptoms, it can generally be relieved readily by division or displacement of the offending vessel.

In the first 841 patients with the presumptive diagnosis of congenital pulmonic stenosis, in whom exploration was carried out, Blalock and associates encountered variations of an aortic vascular ring in 40 instances. The commonest abnormality was a retroesophageal subclavian artery, encountered in 36 patients. It did not appear that these vessels were causing symptoms, but this fact cannot be established with certainty since the basic anomaly causing cyanosis and dyspnea might have masked the symptoms referable to the anomalous vessel.

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In addition to these arterial lesions, a number of venous anomalies have been detected in the course of thoractomy as well as during diagnostic studies employing angiography or catheterization of the heart. These consist of anomalous return of pulmonary veins to the right side of the heart, double superior vena cava, and so-called aneurysm of the vena cava. The surgical significance of anomalous pulmonary vein lesions has been thoroughly discussed by Brantigan and by Findley and Maier.

Intracardiac Septal Defects.—The hemodynamics of experimentally produced interauricular and interventricular septal defects have been studied for many years by Holman and more recently by a number of other investigators. Since there are clinical implications in the production of septal defects as well as in their closure, experimental work has been directed at both aspects of the problem. Experimental production of interauricular septal defects has recently been described by Dodrill and by Blalock and Hanlon. The production of such defects has been employed in the surgical treatment of patients with transposition of the great vessels. Harken and others have used interauricular septal defects as a mechanism for decompressing the left side of the heart in certain cases of mitral stenosis. Experimental work concerning closure of septal defects has been reported by Cohn, Swan, and others. The surgical closure of both interauricular and interventricular septal defects in patients was first reported by Gordon Murray, in 1948. Murray's technique includes the passage of fascial sutures through the heart to form a curtain of interlacing strands, which bridge the defect and make a nidus for clot formation. The indications for operation do not appear to be standardized as yet, and more reports are awaited with interest.

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Cyanotic Heart Disease.—Tetralogy of Fallot: The first report of success in surgical treatment of congenital cyanotic heart disease as typified by the tetralogy of Fallot was made by Blalock and Taussig, in 1945. As is now well known, the operative procedure increases the blood supply to the lungs by means of an extracardiac shunt. The technique of anastomosis between one of the branches of the aorta and the pulmonary arterial system on the right or left side has now become fairly well established together with the ingenious variation of direct aortic-pulmonary anastomosis that was introduced in 1946 by Potts, Smith, and Gibson. Thousands of patients have now been operated on by some variation of these techniques, and enough time has passed so that critical evaluation may now be begun. In general, it may be stated that the formation of an extracardiac shunt for tetralogy of Fallot may be carried out in good risk patients with an immediate mortality of less than 10% and with a high degree of symptomatic relief. It had been feared that there would be a high incidence of cardiac failure in the postoperative period because of the added strain imposed by the artificial ductus arteriosus. Fortunately, this has not proved to be the case, and in most instances postoperative cardiac failure suggests the probability of mistaken diagnosis rather than simple overwork of the heart due to the artificial ductus. When one includes very young infants and those patients with complications such as brain abscess or hemiplegia before surgery, the aggregate mortality including late postoperative deaths may rise to nearly 20%. A policy of not refusing surgery to any patient who may be benefited, despite the desperate risk in some instances, will of course, determine the degree of mortality. Despite such liberal indications for surgery, it has been possible on one occasion to perform a series of anastomoses on more than 40 consecutive unselected patients with the tetralogy of Fallot without a postoperative death. Increasing experience and proficiency in anesthetic management as outlined by Berger play an important role in such a remarkable record.

Because of the acknowledged fact that the shunt adds another abnormality to the tetralogy of Fallot, the possibility of a direct attack on the point of stenosis has long been considered. In 1948, direct attack was successfully introduced by Brock, based on the premise that the infundibular stenosis of the tetralogy is not always a thick-walled process unsuitable for operative modification. At times, the infundibular chamber has at its caudal end a delicate, fibrous ring, which is amenable to resection. Brock has successfully resected a portion of the infundibulum in a small number of cases with beneficial results. The evaluation of patients for direct attack in contrast to an extracardiac shunt is not easy and requires angiography in many instances, in addition to the usual diagnostic tests, together with direct inspection at the time of surgery. It should be noted that in some instances the tetralogy is associated with a valvular pulmonic stenosis rather than an infundibular stenosis, while in other instances both lesions are present. Glover, Bailey, and O'Neill have also employed resection of a portion of the infundibulum, but the exact place of this operation in relation to the more conventional shunting procedures has not yet been established clearly.

Pure Pulmonary Stenosis: Soon after the introduction of the extracardiac shunt treatment of tetralogy of Fallot, it became apparent that this operation was being applied to some patients in whom the underlying pathological condition was pure pulmonic stenosis, rather than the complex group of defects represented by the tetralogy. In "pure" or "isolated" pulmonary stenosis, the interventricular septum is intact. The foramen ovale may be closed or open; in the latter circumstance, severe cyanosis may lead to confusion with tetralogy. It may be emphasized that valvular pulmonary stenosis is generally referred to as "pure" or "isolated" even though blood is being shunted through a patent foramen ovale.

Successful surgical treatment was first performed by T. Holmes Sellors, whose case report appeared after a report of three successful operations by Russell Brock. Since that time, the operation has been carried out with increasing frequency, although the number of patients yet reported is still not large. The latest published report from Brock indicates a mortality of 18% in the last 22 patients, as contrasted with a mortality of more than 50% in his first 11 patients. Blalock and Kieffer have reported division of the stenotic pulmonary valve in 19 patients, with two deaths—one due to severe heart failure and the other to a preexisting abscess of the brain. Improvement in the surgical technique of this procedure associated with the devolepment of new instruments has been reported by Potts, who has successfully operated on a group of infants by this technique.

All these patients have been operated on by the transventricular route, although the technique of approach through the pulmonary artery has been considered by Brock as early as 1948. The technical feasibility of this has been investigated by Brock on a number of occasions, and the technique itself has been employed by Varco, in association with temporary interruption of venous return by occlusion of both venae cavae.

Transposition of the Great Vessels: In this uncommon condition, the great arteries of the heart spring from ventricles opposite to their usual position: the aorta arises from the right ventricle and the pulmonary artery from the left. Since the venous return to the heart is usually normal, the greater and lesser circulations would be completely separate and the patient could not survive extrauterine life unless compensatory abnormalities were present. With increasing clinical experience in the use of angiocardiography in complex cyanotic conditions, the diagnosis is now more often made. A variety of operative attacks has been reported by Blalock and Hanlon in an attempt to improve the compensatory mixing between the two sides of the circulation. These operations have been attended by a discouragingly high mortality, which is justified by the extremely poor prognosis presented by patients with untreated disease. Some success has been obtained by the creation of an interauricular septal defect with or without the creation of an extracardiac artificial ductus arteriosus. It is to be hoped that the development of extracorporeal temporary substitutes for the heart and lungs may permit a definitive surgical correction of this extremely grave abnormality.

Additional Causes of Cyanosis: In addition to peripheral and pulmonary parenchymal causes of cyanosis, there is a variety of lesions that may be responsible for this condition. Among these are pulmonary arteriovenous fistula, anomalous return of a persistent left superior vena cava into the left side of the heart, fistula between the pulmonary artery and the left auricle, and complete return of pulmonary veins to the right side of the heart. The treatment of pulmonary arteriovenous fistula by surgical excision is now well established, and attempts to treat the other entities mentioned have been made with varying degrees of success. The precise evaluation of results in treatment of these unusual lesions is beyond the scope of this presentation.

ACQUIRED LESIONS

Tumors of the Heart.—Primary tumors of the heart are uncommon and are very rarely suspected before postmortem examination. Mahaim has reported 300 cases of intracardiac tumors; in only three was the diagnosis made before death. Many intracardiac tumors, particularly the myxomas, are polypoid and intra-auricular. They would, therefore, be at least theoretically accessible and potentially curable by surgery. At the present time, however, it seems unlikely that the surgical removal of intracardiac tumors will offer a very productive field of endeavor.

Foreign Bodies in the Heart.—The problem of foreign bodies in and about the heart has been well presented by Harken, who operated on a large number of patients with these conditions during World War II. The indications and technique for removal of intracardiac foreign bodies have been elucidated by Harken, who removed 13 such missiles without a death.

Wounds of the Heart.—In penetrating wounds of the heart, death may follow promptly because of cardiac tamponade. The classical treatment by immediate exploratory thoracotomy and cardiorrhaphy resulted in a mortality rate varying from 20% to over 30%. In 1943, Blalock and Ravitch emphasized the importance of pericardial aspiration in the nonoperative management of four patients with cardiac tamponade. Although operation was not resorted to in their cases, they stated clearly that the operating room should be in constant readiness, so that, if aspiration is not successful, a direct exposure and suture of the heart may be performed. In a recent discussion of this subject before the Southern Surgical Association, it was apparent that many experienced surgeons still believe that cardiorrhaphy will be necessary in a not inconsiderable proportion of such cases. This opinion applies particularly to bullet wounds of the heart as compared with stab wounds with a knife or ice pick. In contrast with this viewpoint, it should be stated that Ravitch and Blalock have now accumulated approximately 20 cases of either stab or bullet wounds of the heart in all of which aspiration has been successful. The only fatality in their series occurred several hours after aspiration. At autopsy, a dry pericardial sac was found, but there was a bullet wound of the left anterior descending coronary artery with a fresh myocardial infarct. Aspiration may be carried out on more than one occasion, depending on the clinical response and the rapidity with which blood tends to accumulate. While cardiorrhaphy will undoubtedly be necessary in a small number of patients, such as those with free bleeding into the pleural space, it would appear that the simpler procedure of pericardial aspiration marks a considerable advance in the definitive treatment of patients with acute cardiac tamponade.

Suppurative Pericarditis.—The status of surgery for acute suppurative pericarditis has changed but little since the discussion by Carter in 1948. While the incidence and mortality rate from suppurative pericarditis appear to have declined sharply because of the use of antibacterial agents, the necessity for open drainage remains in many instances. Best results can be expected with combined surgical drainage and antibiotic therapy.

Constrictive Pericarditis.—It has gradually become apparent that many, if not most, cases of chronic constrictive pericarditis are secondary to tuberculous involvement of the pericardium. With this in mind, it has been accepted as axiomatic until recently that operation for removal of the constricting scar should not be undertaken unless all evidence of tuberculous activity has subsided. This opinion has been brought into question by reports of successful operations for removal of the constricting pericardium at a time when the process was obviously active. Holman and Willett have reported five cases of active tuberculosis of the pericardium in which removal of the constricting tissue was attended by excellent results. It now appears proper to carry out operation as soon as evidences of constriction are manifest. By the adoption of such a policy, the operative procedure is rendered easier, safer, and more effective. Moreover, the damaging effect of prolonged constriction is avoided. It

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is apparent that antibiotic medication both before and after surgery plays a large role in the relative impunity with which such major procedures can be carried out in the presence of tuberculous pus without the risk of severe wound infection or generalized dissemination of the tuberculous process.

Various authors have described a number of incisions that are based not merely on surgical convenience but on important theoretical considerations regarding which portion of the heart is more important in initiating the signs and symptoms of constrictive pericarditis. Holman has maintained that decortication of the right side of the heart and the vena cava is of paramount importance, while Churchill has been increasingly impressed with the importance of left-sided cardiac constriction in the causation of symptoms and signs. Both sides of the heart may be approached adequately through a sternum-splitting incision or through an incision such as that proposed by Johnson, which divides the sternum transversely and extends intercostally on either side. The recent publications of Holman have summarized the present state of this evolving problem. Considerable light should be shed on this problem by the investigations of Isaacs and his collaborators, who have produced localized pericardial constriction confined to the right or left side of the heart or, in some instances, to isolated chambers of the heart. Careful physiological studies of animals during the phase of constrictive pericarditis as well as in the postoperative period, after removal of the constriction, should furnish definitive information as to the relative importance of constriction in various areas of the heart in the production of the classical symptoms and signs of this disease.

Coronary Insufficiency.—For over 15 years attempts have been made to relieve myocardial ischemia by improving intercoronary communication or by bringing in an extrinsic blood supply to the heart. The techniques adopted have taken a number of forms: (1) attempts to stimulate the formation of adhesions between the heart and pericardium by means of irritating substances or by physical abrasion; (2) grafting of pedicle flaps of nearby structures, such as lung, omentum, or pectoralis major muscle, on the surface of the heart; and (3) direct anastomosis of systemic blood vessels to the myocardium or to the coronary sinus.

The production of adhesions was carried out by Beck in 37 instances beginning in 1935. During the eight years that these operations were carried out, there were 23 patients who survived, of whom all but 4 showed some degree of improvement. Thompson subsequently reported similar efforts with the application of talcum to form adhesions between the heart and the pericardium. In his latest report on 38 patients, Thompson reported 70% good results and a mortality rate of just below 16%.

Although it is undoubtedly true that adhesions form under the stimulus of such irritation, considerable doubt has been expressed as to whether such adhesions continue to carry blood after the passage of some time. Objection has also been raised concerning the vascular connections that have been demonstrated between the myocardium and the various structures that have been grafted on it. Although postmortem injection through such channels reveals wide patency, it is uncertain to what degree and in what direction the blood has been flowing during life.

In a recent publication, Beck and his co-workers have presented a progress report on their researches in revascularization of the heart. Their current technique consists in directing arterial blood into the coronary sinus by means of a free vein graft between the aorta and coronary sinus. It is important to restrict the arterial inflow by making an aortic stoma that is no larger than 3.5 to 4 mm. in diameter. The total ligation of the coronary sinus as a preliminary, simultaneous, or subsequent procedure has been abandoned, because it introduces so much blood into the venous tree that the pressures rise excessively and thereby reduce blood flow, with thrombosis of the grafts. However, it has been considered advisable at a second stage to constrict the outflow from the coronary sinus to a diameter of 3 mm.; in 12 of 13 dogs subjected to this two stage procedure, there has been protection against the lethal effects generally seen in occlusion of the anterior descending branch of the left coronary artery at its point of origin.

The initial patient operated on by Beck, employing this general technique in 1948, died. However, in February, 1949, Beck described two patients in whom this procedure had been successfully carried out. The ultimate result in these patients will require more prolonged evaluation.

In a theoretical consideration of Beck's operation for clinical cases of myocardial ischemia, the question has been raised as to the actual occurrence of retrograde flow of arterial blood in the coronary venous system when the coronary sinus is only partially occluded. It is Beck's contention that the protection afforded against reduced coronary arterial inflow by the usual channels demonstrates that arterial blood must be reaching the myocardial bed by the new route. Heimbecker, Thomas, and Blalock have shown that flood flow, at least temporarily, may be reversed in the capillaries of the intestine, but doubt has been expressed as to whether this occurs in the myocardium under the circumstances noted.

Some hesitancy has been expressed in accepting a procedure involving two vascular anastomoses, because of the fear that patients who needed this operation might possibly not survive so extensive a procedure. In order to overcome this objection, Vineberg has devised an operation of implanting the internal mammary artery into the myocardium and has tested the feasibility of this procedure by extensive researches in the experimental laboratory. It is Vineberg's contention that what one needs is a quick and simple procedure. In April, 1951, he described four patients in whom this procedure had been tried. One patient died, two were said to show benefit, and the last had been operated on too recently for evaluation.

Valvular Lesions.—Mitral Stenosis: At the present time direct attack on the mitral valve is the preferred therapy of mitral stenosis, in contrast with the technique of sympathectomy or intracardiac or extracardiac shunts. In the initial stages of the work on mitral stenosis, it was believed that some degree of regurgitation must be exchanged for the severe degree of stenosis. The surgical attack on the mitral valve, however, is now designed to

split or cut the valve along the so-called commissures and thereby produce some approximation of normal valvular function. Particular care must be taken to preserve the integrity of the valve leaflets, particularly the anterior leaflet, in order that fatal regurgitation may not occur. The left auricular route to the mitral valve is generally preferred to an approach through the pulmonary veins or the transventricular approach. There are two main methods for restoring the valve to some semblance of its previous integrity. In the first of these (Bailey's "commissurotomy"), one cuts the fusion areas of the cusps at either the anterolateral or posteromedial area; in some instances, both commissures are divided. The second technique, which is known as dilatation or "finger-fracture," accomplishes the same result by digital manipulation, with probably a greater risk of tearing one of the cusps in an area away from the commissure.

The selection of patients for surgery with particular reference to indications and contraindications forms a large problem, on which data are being accumulated rapidly. The ideal patient for surgery appears to be a young person, well below the age of 40, with little or no cardiac enlargement, with a regular rhythm, with no evidence of rheumatic activity or of subacute bacterial endocarditis, and with a mitral stenosis with minimal or no regurgitation, and without lesions of other valves. The presence of fibrillation is not an absolute contraindication; some patients with this condition may have a normal rhythm after successful surgery. A history of repeated embolization is considered of bad prognostic import, although one may ligate the left auricular appendage at its base after manipulations on the mitral valve and thereby prevent the development of future emboli. It should be noted that, aside from the incidental ligation of the auricular appendage in the course of mitral valvulotomy, this procedure has been recommended as a preventive for recurrent emboli originating in the left as well as in the right auricle. The operation of mitral valvulotomy would appear to be contraindicated in the presence of active rheumatic carditis or extreme cardiac enlargement and cardiac failure which does not respond to the customary measures. Bailey and his co-workers have now operated on approximately 200 patients, with an over-all mortality of about 10%. This includes the initial mortality, which, of course, was high. It is estimated by Dr. Bailey, on the basis of a short-term follow-up, that approximately 75% of the survivors are somewhat improved. In some instances this amounts to a clinical cure, while in others the improvement has been only moderate. It is a striking fact that laboratory data, such as a pulmonary function and cardiac output, may show only minimal degrees of improvement, while the clinical improvement may be very pronounced. In some instances, a successful valvulotomy may be attended by negligible improvement because of severe pulmonary fibrosis, which is often associated with long-standing mitral stenosis. In other cases, myocardial insufficiency may not allow the resumption of a normal cardiac output even though the mechanical obstruction may have been radically improved. A number of investigators, such as Blalock, Brock, and Harken, have operated on sizable numbers of patients with results comparable to those of Bailey and his associates.

Experimental work has been carried on by Templeton, Gibbon, and others with a view to replacement of damaged valves by substitutes formed of vein grafts and pericardium. Gordon Murray has carried out similar work in patients, and, more recently, Bailey and his co-workers have modified Murray's technique in an attempt to relieve the effects of mitral regurgitation either naturally occurring or artificially produced at the time of operation for mitral stenosis. It is too early to evaluate the results of these preliminary attempts at correction of mitral regurgitation.

Aortic Stenosis: Coincident with the reasonable success attained in the treatment of mitral stenosis, a number of investigators turned their attention to surgical relief of aortic stenosis. The first person to be treated successfully by surgery for this condition was operated on in 1914 by Tuffier, who dilated a stenotic aortic valve without opening the aorta. The patient was alive and getting along satisfactorily 10 years after this procedure. In the ensuing years, there was considerable activity by Cutler, Levine, and Beck, Horace Smithy, and others. Smithy divided the aortic valve in animals by an aortic approach using a small knife. In 1947, Brock inserted an operating cardioscope through the divided right subclavian artery and passed it down to the aortic valve, with a view to dividing an aortic stenosis. The valve was found to be calcified, however, and the attempt was abandoned without disturbing the patient. In April, 1950, Bailey and his co-workers presented a report of two patients with aortic stenosis whose aortic valves had been dilated by means of a special dilator inserted through the great vessels in the neck. They also reported a division of the aortic valve in one instance by a transventricular approach, which resulted fatally because of regurgitation. In a later report, in which these three patients were described and their experiences with the experimental approach to this problem were reviewed, they added two additional cases. In one of these, the approach had been through the ventricle, with successful dilatation of the stenotic valve; in the other, death resulted from the production of a false passage as the instrument was passed from above. A number of other unreported attempts at aortic valvulotomy have been made with generally discouraging results, because of the notorious tendency of these patients to ventricular fibrillation. It may be said that the surgical therapy of aortic stenosis is in a discouraging state at the present time, but further advances may brighten this picture considerably.

COMMENT

It is apparent that individual surgical advances have been made possible by basic advances in diagnosis, anesthesia, cardiovascular physiology, and postoperative care. Research is now proceeding rapidly along a number of lines that offer opportunity for still greater progress. It is possible to mention these only briefly.

The grafting of blood vessels introduced by Carrel and others a generation ago has been brought to a high degree of refinement by recent investigators. Gross, Bill, and Peirce have employed preserved aortic grafts in a number of patients on the basis of admirably thorough experimental studies. The feasibility of a blood vessel bank was indicated by this work. Keefer and others, in a

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cooperative venture in the New York area, have demonstrated the practicability of a blood vessel bank as an outgrowth of the work of Gross and others. Although the needs will never be comparable to those for blood and plasma, it is to be expected that in the future such blood vessel grafts will be available from a central bank or multiple banks in large metropolitan areas in much the same way that blood is now dispensed. The ready availability of such grafts will undoubtedly extend widely the scope of excisional and reparative surgery in the future.

Much effort has been expended to determine the best method for preservation of such grafts in a viable state. Recently, it has been shown that tissues may be preserved without gross damage by lowering the temperature extremely rapidly and thereby avoiding the damaging effects of freezing. Such "vitrification" has been applied successfully to isografts of skin. Of considerably greater importance would be an explanation of the factors responsible for failure of grafts from one patient to another. A satisfactory solution of this biologic problem, particularly in relation to more complex tissues or entire organs, would open an entirely new era in surgical research. In the meantime, various expedients, such as replacement of blood vessels with plastic substitutes, have been carried out, and, in some instances, prosthetic valves have been fashioned for use in experimental animals to replace the aortic or mitral valve. The necessity for such ingenious devices would be largely obviated if the problems of homotransplantation of tissues were solved.

From the technical standpoint, the most serious deterrent to definitive repair of cardiovascular defects has been the necessity for maintaining the pumping action of the heart and the oxygenating function of the lung. A variety of fairly efficient pumps has been devised to take the place of either the right or left side of the heart. Much more complex, however, is a machine that will substitute for the function of the entire heart and lungs. The researches of Gibbon and his associates and of Jongbloed, Bjork, Dennis, and others have solved many of the basic problems in this field, and the apparatus has been successfully applied in animals for a number of years. Initial clinical trials have been described by Dennis, Varco, and others, and it is anticipated that more extensive clinical application will soon be reported. Widespread use of such an apparatus should have an incalculable effect on the future of cardiovascular surgery.

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DIAGNOSIS OF INFECTIOUS MONONUCLEOSIS

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The incidence of positive heterophil tests in infectious mononucleosis is a much disputed point. The present day consensus in regard to this question can be epitomized. as follows: A minor but substantial percentage of patients with infectious mononucleosis have diagnostic blood smears but negative heterophil reactions; therefore, a positive heterophil reaction is a desirable adjunct but not essential to the diagnosis. It is often difficult to ascertain just how serious an attempt has been made to diagnose these cases serologically. If these seronegative cases are classified on the basis of a single negative reaction obtained during the first seven days of the illness, the results are understandable. In my experience all patients with infectious mononucleosis characterized by a positive blood smear have shown a diagnostic titer of heterophil antibodies, provided the blood was tested serially through the second week of the disease.

MATERIAL

This study is based on observations on 146 hospitalized and 194 ambulatory patients whom I followed up both clinically and hematologically. These patients were all college students, aged 17 to 32 years, and all were seen at the Hall Health Center, University of Washington, after January, 1946.

Atypical cases of infectious mononucleosis, presenting diagnostic difficulties, are not rare. While 96% of the cases in this series were recognized clinically because of the familiar anginose pattern, there were 13 patients in whom the diagnosis was not immediately apparent; the diagnosis was made only after several days' observation, chiefly on the basis of laboratory findings.

LABORATORY FINDINGS

The early white blood cell counts ranged from 4,100 to 37,400. In 83 patients examined during the first week the average was 8,000 white blood cells. Only five patients in this group had counts of less than 6,000. The average total white blood cell count at the peak of the illness was 15,500.

A blood smear was considered diagnostic when the absolute atypical lymphocyte count was greater than 1,000 per cubic millimeter. However, this, by itself, is not an indication for the diagnosis of infectious mononucleosis. More adequate differentiation of the mononuclear cells by means of supravital staining is necessary, since this number of atypical lymphocytes may indicate rubella, rubeola, varicella, or mumps.

Standard references on hematology contain excellent illustrations of the familiar large atypical lymphocyte with vacuolated cytoplasm known as the Downey Type I cell. This cell was present in somewhat over 90% of smears in my series. While the Type III Downey cell is not rare, in my experience it has been necessary only once to consider seriously acute lymphatic leukemia in the differential diagnosis. The white blood cell count in this case was 45,300; the differential count showed 9 segmented neutrophils, 8 stab forms, 22 lymphocytes, and 61 abnormal lymphocytes, over one-half of the last group showing well-formed nucleoli. This patient was seen in 1941 and is not included in this series.

Approximately 8% of the patients in this series have had atypical lymphocytes of a type I have not seen

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described. The over-all size is about that of the average Type I cell; the cell outline, however, varies widely and is probably best described as scalloped or irregular. The nucleus is usually angular and frequently truncated, extending across the cell from side to side, bisecting the cytoplasm. The nuclear chromatin is diffuse and does not resemble the Type II cell, as illustrated in plate 1, figure 7, in Downey's paper.[1] The cytoplasm may contain a few inclusions but generally is agranular; it has a very delicate reticular structure, usually brownish gray, but, as the cytoplasm approaches the cell membrane, both become basophilic.

The prime feature making identification unmistakable, however, is the cellular outline. It frequently projects itself as pseudopodia in three or four directions, to a distance of 4 to 8 μ, between adjacent red blood cells. In somewhat thicker sections of the smear the cytoplasm will be deeply scalloped by the red blood cells. This unnatural susceptibility to pressure is seen in the nucleus as well, when it is eccentrically positioned. Thus it would seem that this cell is structurally weak, resulting in bizarre configurations, a feature not seen in other types of atypical lymphocytes. I do not intend to infer that this cell picture is the result of anything besides the polychrome staining technique; I have never observed its counterpart in supravital preparations.

*Initial Heterophil Titers in Fifty-Seven Cases of Infectious Mononucleosis**

Initial Heterophil Titers	Day of Illness								
	4	5	6	7	8	9	10	11	12
1:14,336	..	..	1†	..	..	..	..	..	1†
1:7,168	..	..	..	..	1	1†	1	1†	1†
1:3,584	..	..	..	1	1†	1	1	1	2
1:1,792	..	..	1†	1	2	..	..	1	..
1:896	..	..	..	..	..	..	2	..	1
1:448	..	3	1	1	2	3	1	1	..
1:224	..	1	..	4	1	..	..	..	..
1:112	..	1	1	3	2	..	..	..	..
1:56	..	3	..	..	..	..	..	..	..
1:28	..	..	1	..	..	..	..	..	..
1:14	2	..	2	..	..	..	..	..	..
1:7	1	1	..	..	..	..	..	..	..

* In these cases it was possible to determine the exact time of onset of clinical signs and symptoms. There was a rise in subsequent titers in all cases except those marked with a dagger (†).

It is to be emphasized that the atypical cells seldom present recognizable characteristics in smears prepared for routine differential counts. Under these circumstances the abnormal cells cannot be distinguished from normal lymphocytes. The characteristics of the cytoplasm are all but completely obscured; on the other hand, a thin even spread makes these cells easy to identify. This may appear to be elementary and unnecessary emphasis, but this thin smear technique is not generally practiced or properly appreciated.

My co-workers and I have selected a heterophil titer of 1:56, read macroscopically, as being positive. Only 11 patients had this low titer; three were seen only during convalescence; and eight were examined only once at the onset and thereafter did not consult us. However, all had diagnostic blood smears. Actually I have not encountered patients continuously under my care in whom the titer remained so low. In very few hospitalized patients does a titer of 1:896 fail to develop. A titer of 1:114,708 was recorded once; this subsided in fairly regular increments and was 1: 224 after three months.[2]

It is of some practical importance to know how soon after the onset of the disease one can expect a positive heterophil reaction. Although special attention was given to the mode and time of onset of the illness, I was able to determine the time accurately in only 57 cases. Only instances in which the patient could definitely date the onset within a period of a few hours were used in compiling the accompanying table. It would appear that if the heterophil titer is not positive at the beginning of the second week other leads should be pursued.

SEARCH FOR CASES

Since 1946, I have done heterophil tests on many patients whose illness, because of one feature or another, simulated infectious mononucleosis. In my work with students an excellent opportunity is afforded for observation of many patients with infectious diseases very early. My attention was attracted to one group chiefly because of signs suggesting infectious mononucleosis; included in this group were many cases of acute respiratory disease, tonsillitis due to streptococcic involvement or Vincent's organisms, rubella, mumps, toxic erythema, penicillin reactions, Hodgkin's disease, adenopathy secondary to local infection, and herpetic gingivostomatitis. Another group studied presented a blood picture slightly suggestive of infectious mononucleosis but failed, as in the above group, to show heterophil antibodies. These included infectious hepatitis, influenza, malaria, serum reactions, lymphatic leukemia, common cold, and aplastic anemia. The easy availability of our medical service made it possible to follow many patients from day to day and to ultimately make a definitive diagnosis, when the initial findings were not sufficiently characteristic to do so.

The prevailing opinion holds that a negative heterophil reaction in the presence of suggestive clinical signs should not deter one from making a diagnosis of infectious mononucleosis. This may result in a diagnosis of infectious mononucleosis with bizarre symptomatology.

In a disease with such protean manifestations the question arises as to just what constitutes clinically significant signs and symptoms. For example, is a diagnosis of infectious mononucleosis justified when hepatitis and headache or when fatigue with vague aches and pains plus a borderline blood smear constitute the clinical picture? In some quarters there is a tendency to make the diagnosis of infectious mononucleosis in such a situation. Each year I have followed one or two such cases. In 1947 I followed three patients with a fatigue, ache, and pain syndrome, each for 14 weeks. In addition to having daily temperature records, these patients were examined three times weekly, a white and differential blood cell count was done twice weekly, and the heterophil titer was determined once weekly. The heterophil titer never exceeded 1:14. The differential counts showed a peak of 55% lymphocytes but averaged 45%; none to 280 atypical lymphocytes were recorded. For a week at the onset, afternoon temperatures were elevated

1. Downey, H., and McKinlay, C. A.: Acute Lymphadenosis Compared with Acute Lymphatic Leukemia, Arch. Int. Med. 32:82 (July) 1923.

2. Since this series was completed, the exceedingly high titer of 1:1,832,448 was obtained for a 19-year-old female student being treated with corticotropin. Differential absorption tests for this patient were specific for infectious mononucleosis.

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one-half to one degree, but positive physical signs were nonexistent.

This type of case is not included in this series. The symptoms, afebrile course, and absence of signs were not the only atypical features. The white blood cell counts never exceeded 8,300, and the smears could hardly be considered even borderline. Whether one can disregard repeatedly negative heterophil titers and make the diagnosis of infectious mononucleosis from a combination of neurasthenic symptoms and a slightly abnormal blood smear is questionable.

CONCLUSION

My experience during the past five years has indicated that seronegative infectious mononucleosis in this age group (17 to 32 years) must be rare indeed. I have demonstrated a positive heterophil titer in all patients having a positive blood smear. The lymphocytosis of rubella or mumps or that occurring during convalescence from acute infections and numerous chronic illnesses is understandably not accompanied by a positive heterophil reaction. Special attention has been focused on isolated smears showing 50% to 55% lymphocytes. Not all patients with this percentage of lymphocytes have infectious mononucleosis. However, if careful examination shows that more than 1,000 of these are abnormal lymphocytes, the heterophil titer has been positive.

Some physicians treating older groups believe that negative heterophil antibody titers are not uncommon in infectious mononucleosis. They believe that the number of seronegative cases is not inconsiderable and that antibody titers may vacillate unpredictably. I question whether the presence of sheep cell agglutinins are as unpredictable as some have thought. Experience gained during the past five years in following the rise and fall of heterophil antibodies by serial determinations in a large number of patients has increased my confidence in this procedure.

I have been impressed by the atypical symptoms, absence of signs, and negative heterophil reactions in many patients showing lymphocytosis but a lack of atypical lymphocytes. Some physicians may be trying too hard to pigeon-hole the cases in which there is only an ephemeral lymphocytosis. My conception of the seronegative state may change as soon as I encounter a straightforward example of infectious mononucleosis with sore throat, adenopathy, and a diagnostic blood smear that fails to develop a respectable titer of sheep cell agglutinins after multiple determinations.

We all are willing to accept the diagnosis when the smear is diagnostic and heterophil antibodies are positive even though the clinical picture is a bit bizarre. However, it would seem to be an entirely different matter when the blood smear shows only lymphocytosis and the antibodies are absent too.

In spite of numerous atypical clinical pictures, it is well to recall that sore throat and adenopathy represent the clinical prototype in this disease. For the present it would seem wise to insist on more strict rather than less strict serologic and hematologic findings when they are absent.

SUMMARY

Studies on 340 college students with infectious mononucleosis have indicated that a seronegative finding in this age group must be rare indeed. I have been successful in obtaining a positive heterophil antibody titer in all cases with diagnostic smears. Evaluation of a group of patients with atypical symptoms, absence of signs, and certain hematologic and serologic deficiencies that hardly warrant the diagnosis of infectious mononucleosis is discussed.

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CLINICAL AND PATHOLOGICAL CONSIDERATIONS IN CASES OF CALCIFIC AORTIC STENOSIS

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Chronic cardiac disease due to, or associated with, calcific aortic stenosis is encountered frequently in the practice of internal medicine. Calcific aortic stenosis is an entity of clinical significance either when it produces symptoms of cardiac malfunction or when it appears as an asymptomatic complication. Public health measures and improved medical care have increased longevity in this country. Since calcific aortic stenosis is largely a lesion that comes to the fore in middle life or old age, it now is met frequently.

Much of the literature concerning calcific aortic stenosis has pertained to the controversy concerning the cause of this valvular deformity. Dry and Willius [1] and later, Karsner and Koletsky [2] added strong evidence favoring rheumatic fever as the causative factor. Other authors have presented evidence in favor of a nonrheumatic origin.[3] It is possible that, in some instances, the resultant valvular deformity may be due to a combination of phenomena.[4]

In 13 of the 49 cases here reviewed, we obtained a history of rheumatic fever. The original episode occurred 13 to 62 years before death, and the average period of survival after acute rheumatic fever was 35.6 years in this group. We will not attempt to clarify causation further in this paper by seeking to classify our cases into examples of Mönckeberg's aortic valvular sclerosis and healed rheumatic valvular deformity.

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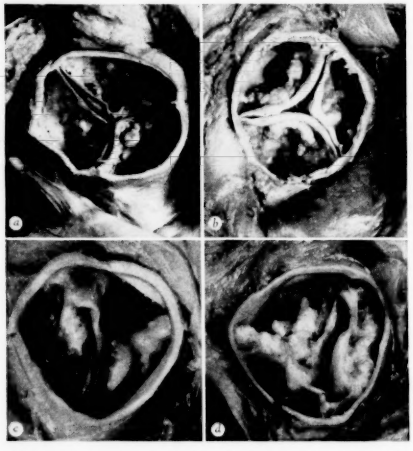
From the Division of Medicine (Dr. Anderson) and the Section of Pathologic Anatomy (Dr. Edwards), Mayo Clinic; Fellow in Medicine, Mayo Foundation, University of Minnesota (Dr. Kelsey).

1. Dry, T. J., and Willius, F. A.: Calcareous Disease of the Aortic Valve: A Study of 228 Cases, Am. Heart J. **17**: 138-157 (Feb.) 1939.

INVESTIGATIVE MATERIALS AND METHODS

We reviewed the clinical records, necropsy specimens and records, and electrocardiograms in 49 cases in which calcific aortic stenosis was demonstrated at necropsy. These observations are of a similar type to those of an earlier study made at the Mayo Clinic on a larger series of patients.[1] All our patients had complete examinations at the clinic during life, and in 38 (77.5%) the clinical diagnosis of aortic stenosis was made as either a primary or a secondary diagnosis before death. In our cases we did not include any instances of significant valvular deformity other than that of the aortic valve, which militates against our attempting an etiological study. Forty-seven of the 49 patients had multiple lead electrocardiograms.

The clinical records were examined, and symptoms of coronary insufficiency, cardiac decompensation, and myocardial infarction, together with such events as syncope, convulsions, and sudden death were recorded.



The aortic valve photographed from the aortic side in cases of calcific aortic stenosis graded according to the classification in the text: *a*, aortic stenosis, grade 1; *b*, aortic stenosis, grade 2; *c*, aortic stenosis, grade 3; and *d*, aortic stenosis, grade 4.

These records also were used to gather information concerning physical findings, complicating illnesses, and surgical experiences in the group. These clinical features were correlated with the electrocardiographic findings and with the pathological findings. We examined each heart carefully to assess the severity of the aortic stenotic process, to determine the status of the coronary arterial circulation, and to observe the presence, or absence, of myocardial infarction.

We have classified the degree of aortic stenosis as follows (see the accompanying figure): In grade 1, aortic stenosis, moderate rigidity and calcification of the aortic cusps with minimal or no fusion at the commissures were present; in grade 2, moderate rigidity and calcification of the aortic cusps with fusion at one commissure; in grade 3, marked rigidity but still with some flexibility and marked calcification of the aortic cusps with fusion of two commissures; and grade 4, pronounced rigidity without flexibility and decided calcification of the aortic cusps with fusion of at least two commissures and minimal ostium for ejection of blood.

Coronary occlusive disease was similarly classified according to the greatest degree of narrowing in the entire coronary tree, as follows: Coronary sclerosis was graded 1 when the diameter of the lumen was narrowed less than 25% from normal; graded 2 when it was narrowed 25% to 50%; graded 3 when it was narrowed 50% to 75%; and graded 4 when it was narrowed more than 75%. In instances in which a small segment of the coronary arterial tree had a greater occlusive process than the remaining coronary circulation, we have classified the degree of coronary sclerosis the same as the degree of occlusion of the most involved segment.

OBSERVATIONS

General Features.—Forty-one (83.7%) of the 49 patients were men and 8 (16.3%) were women. The age at death varied from 39 to 90 years for the entire group, and the average age at death was 63.4 years. According to our criteria, 11 patients had grade 4 aortic stenosis, 20 had grade 3, 11 had grade 2, and 7 had grade 1. The ages according to decades and sex are presented in table 1.

Coronary Insufficiency.—The incidence of symptomatic coronary insufficiency was high in our series of cases, as was the incidence in previously reported cases.[5] We accepted as clinical evidence for coronary insufficiency a history of recurring pain in the thorax induced by sustained physical effort. In 20 of our 49 cases (40.8%), angina pectoris had occurred. The duration of angina prior to death ranged from three months to 15 years, with an average duration of about 43 months. There was no significant age difference between patients who had angina and those who did not have that symptom. Our findings on examination of the hearts are given in table 2.

These observations indicate a greater incidence of a severe degree of coronary occlusive disease in those patients with angina as compared with those without angina (40% versus 13.8%). They also show that 11 of the 13 patients who had angina with advanced states of aortic stenosis had minimal coronary atherosclerosis. This suggests that the symptoms of coronary insufficiency were related primarily to the stenotic valve in these cases. It is of interest, however, that the incidence of severe aortic stenosis with mild coronary sclerosis was the same among patients with and without angina.

Myocardial Infarction.—In the clinical data, episodes of prolonged myocardial ischemia, at various intervals prior to death, were diagnosed by the clinicians as myo-

2. Karsner, H. T., and Koletsky, S.: Calcific Disease of the Aortic Valve, Philadelphia, J. B. Lippincott Company, 1947.

3. (*a*) Sohval, A. R., and Gross, L.: Calcific Sclerosis of the Aortic Valve (Mönckeberg Type), Arch. Path. **22**: 477-494 (Oct.) 1936. (*b*) Friedberg, C. K., and Sohval, A. R.: Nonrheumatic Calcific Aortic Stenosis, Am. Heart J. **17**: 452-469 (April) 1939.

4. Sophian, L. H.: Calcific Aortic Valvular Stenosis, Am. J. M. Sc. **210**: 644-652 (Nov.) 1945.

5. (*a*) Dry and Willius.[1] (*b*) Contratto, A. W., and Levine, S. A.: Aortic Stenosis with Special Reference to Angina Pectoris and Syncope, Ann. Int. Med. **10**: 1636-1653 (May) 1937. (*c*) Clawson, B. J.; Noble, J. F., and Lufkin, N. H.: The Calcified Nodular Deformity of the Aortic Valve, Am. Heart J. **15**: 58-76 (Jan.) 1938. (*d*) Reich, N. E.: Calcific Aortic Valve Stenosis: A Clinicopathologic Correlation of 22 Cases, Ann. Int. Med. **22**: 234-251 (Feb.) 1945. (*e*) Hammarsten, J. F.: Syncope in Aortic Stenosis, A.M.A. Arch. Int. Med. **87**: 274-279 (Feb.) 1951.

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cardial infarction 12 times in eight cases. In only one case was myocardial infarction the immediate cause of death.

Evidence that prolonged periods of coronary insufficiency may occur in patients with calcific aortic stenosis without gross infarction of the myocardium is the observation that in only 4 of 49 hearts was gross evidence of healed or acute infarction found on examination. In many hearts, however, there were scattered multiple small scars. In three of the four hearts in which gross myocardial infarction was noted, severe coronary atherosclerosis (grade 3 to 4) with minor degrees of aortic stenosis (grade 1 to 2) was evident. In the fourth heart in which healed myocardial infarction was found at necropsy, severe aortic stenosis with minimal coronary occlusive disease was present. The electrocardiographic picture was diagnostic of myocardial infarction in three of the four cases in which pathological findings were positive. The electrocardiographic patterns of the four additional patients for whom a clinical diagnosis of myocardial infarction had been entertained were equivocal.

TABLE 1.—*Age and Sex Distribution of Forty-Nine Patients Who Had Calcific Aortic Stenosis**

Decades	Total No. of Patients	Men	Women
30-39	1	1	0
40-49	5	5	0
50-59	12	10	2
60-69	17	13	4
70-79	8	7	1
80-89	5	4	1
90-99	1	1	0
Total	49	41 (83.7%)	8 (16.3%)

* The average age at death was 63.4 (63.2 for the men and 64.2 for the women). The total age range at death was 39 to 90 years.

The correlation of clinical, electrocardiographic, and pathological diagnoses of myocardial infarction in cases of calcific aortic stenosis in this small group has not been good. We have attributed this to the apparent occurrence of prolonged yet reversible myocardial ischemia indistinguishable clinically from myocardial infarction, together with the frequent presence of electrocardiographic aberrations, such as left bundle branch block, which decrease the value of the electrocardiogram when a diagnosis of myocardial infarction is attempted.

TABLE 2.—*Incidence of Degrees of Aortic Stenosis and Coronary Sclerosis*

	Angina		No Angina	
	Number	%	Number	%
Aortic stenosis, grade 3 or 4				
With coronary sclerosis, grade 3 or 4	2	10.0	2	6.9
With coronary sclerosis, grade 1 or 2	11	55.0	16	55.2
Aortic stenosis, grade 1 or 2				
With coronary sclerosis, grade 3 or 4	6	30.0	2	6.9
With coronary sclerosis, grade 1 or 2	1	5.0	9	31.0
Total	20	40.8	29	59.2

Myocardial Failure.—Myocardial failure was an extremely prominent feature. We have accepted as evidence of myocardial failure a history of increasing dyspnea with mild exertion, the occurrence of paroxysmal nocturnal dyspnea, and episodes of acute pulmonary edema, in addition to chronic congestive failure manifested by peripheral edema and hepatomegaly. Failure of the left ventricle, as expected, was the primary event in all cases of chronic cardiac decompensation.

By our criteria myocardial failure occurred in 36 of the 49 cases (73.5%), the duration of failure prior to death ranged from seven days to 11 years, and the average survival after the onset of myocardial failure was 2.2 years. Five patients survived more than five years after the onset of myocardial failure, and 14 died within one year. Further observations relating to the pathological and clinical findings in the presence or absence of myocardial failure are given in table 3. Little measurable difference was found in the two groups. In cases of myocardial failure the hearts were slightly heavier and, also, hypertension was recorded more frequently, while patients who did not have myocardial failure prior to death survived a few years longer, on the average, than the others.

Sudden Death, Syncope, and Convulsions.—The occurrence of syncopal attacks and convulsive seizures punctuating the course of calcific aortic stenosis has been described frequently. These dramatic episodes have been attributed to cerebral anoxia associated with diminished cardiac output,[5a] disturbances of cardiac conduction,[6] and hypersentitive carotid sinus.[5b] Sudden and unexpected death is likewise a peculiarity observed in these cases. In contrast to other studies in which the incidence has been considerably higher, convulsive seizures occurred in only two of our 49 cases and syncope in only three. One of the patients who had convulsive episodes had complete auriculoventricular dissociation, observed by electrocardiography, with frequent Adams-Stokes seizures, but in the others with syncopal and convulsive disturbance there was no electrocardiographic abnormality to explain the events.

TABLE 3.—*Clinical and Postmortem Observations in Patients With Myocardial Failure*

	Myocardial Failure		No Myocardial Failure	
	Number	%	Number	%
No. of patients	36	73.5	13	26.5
With angina pectoris	16	44.4	4	30.8
With hypertension	11	30.6	1	7.7
Aortic stenosis, grade 3 or 4				
With coronary sclerosis, grade 3 or 4	3	8.3	1	7.7
With coronary sclerosis, grade 1 or 2	19	52.8	8	61.5
Aortic stenosis, grade 1 or 2				
With coronary sclerosis, grade 3 or 4	6	16.7	2	15.4
With coronary sclerosis, grade 1 or 2	8	22.2	2	15.4
Weight of heart, gm.				
Average	628		595	
Range	390-995		385-935	
Average age at death, yr.	62.8		65.9	

Eleven patients died suddenly. Pathological study did not reveal significant differences in hearts of these 11 patients from the hearts of the others. Nine of the 11 had severe aortic stenosis, grade 3 or 4, and one of these nine had associated severe occlusive coronary disease. The other two had severe coronary atherosclerosis with minimal aortic stenosis, which suggests that the coronary disease was responsible for death.

6. Boas, E. P.: Angina Pectoris and Heart Block, as Symptoms of Calcareous Aortic Stenosis, Am. J. M. Sc. **190**: 376-383 (Sept.) 1935.

General Physical Findings.—A diagnosis of aortic stenosis is easily made from findings at physical examination when all the classical physical findings, including a palpable systolic thrill and harsh murmur in the aortic area, absence of the second sound in the aortic area, and a slowly rising and falling pulse, are observed. When there is severe congestive failure with diminished cardiac output or when there is advanced emphysematous changes in the lungs, both of which obscure the characteristic cardiac findings, aortic stenosis may be overlooked.

TABLE 4.—*Electrocardiographic Abnormalities in Cases of Calcified Aortic Stenosis*

Type of Disturbance or Abnormality	No.
Rhythm	
Auricular fibrillation	5
Auricular flutter	1
Complete heart block	1
Terminal ventricular tachycardia *	1
Conduction	
P-R interval greater than 0.2 sec.	8
Left bundle branch block	6
Right bundle branch block	2
Complete heart block	1
Myocardial changes †	
Left ventricular hypertrophy and strain	24
Diffuse myocardial damage	9
Relic of myocardial infarction	4
Digitalis effect	4
Pulmonary embolism	2

* Previous sinus rhythm.
† In some cases more than one abnormality was noted.

We have attempted to evaluate only the characteristic aortic systolic murmur, the thrill, and the aortic diastolic murmur in our series, because of the infrequency with which the clinician has commented on the pulse and aortic second sound. A clinical diagnosis of aortic stenosis was made in 38 (77.6%) of the 49 cases. Thirty-one (63.2%) patients gave histories of previous knowledge of a murmur, having known of its existence for nine months to 43 years. There was no apparent relation between the severity of the aortic stenosis and the duration of the murmur.

A systolic thrill was noted in 17 patients (34.7%). As anticipated, 15 of these patients had severe aortic stenosis, grades 3 and 4. Ten (58.8%) of the patients in whom aortic thrills were observed had angina pectoris, although only two had severe coronary atherosclerosis.

When the valvular deformity is sufficiently severe to hinder closure of the aortic valve during ventricular diastole, aortic regurgitation, with its characteristic murmur, is found. We observed the aortic diastolic murmur in 16 cases (32.6%). The incidence of symptomatic coronary insufficiency and increased cardiac weight are not greater in this group than in the group without recorded diastolic murmurs.

Electrocardiographic Findings.—As said before, one or more electrocardiograms with multiple leads were made in 47 of our 49 cases. In only five patients was the electrocardiographic pattern considered to be within the limits of normal in all respects. It is noteworthy that the average weight of the hearts in the five patients without electrocardiographic abnormality was 450 gm., whereas the average weight of the hearts for the whole series was more than 600 gm. Only two of these five patients had myocardial failure. In both, this was manifested by acute pulmonary edema leading to death. Death was attributed to metastatic cancer in two of the other three patients and to pulmonary embolism in one. Aortic stenosis was severe in four of the five, and in none was there severe coronary sclerosis. In the other 42 cases in which electrocardiograms were made varied types of electrocardiographic abnormality were manifested by patterns indicating disturbances of rhythm or conduction or myocardial injury (table 4).

Our observations revealed no constant pattern of electrocardiographic abnormality. This is in keeping with the experience of others.[7] The most frequently observed electrocardiographic variants are patterns indicative of left ventricular hypertrophy and strain and left bundle branch block. One or the other of these appeared in 30 of 47 cases (63.8%). These changes also are prominently seen in cases of other vascular lesions, such as syphilitic aortic insufficiency and arterial hypertension, which produce increased work on the part of the left ventricle. Left ventricular hypertrophy and strain, and left bundle branch block, therefore, are manifestations associated with progressive thickening of the myocardium of the left ventricle regardless of the cause.

The incidence of auricular fibrillation in our group was surprisingly small (10.2%) and somewhat less than that reported by other observers.[8] This difference may be related to selection, as we eliminated patients who had associated gross mitral disease.

Nine patients had electrocardiographic patterns that we have listed under the poorly defined term "myocardial damage," for want of a more concise term. In this "wastebasket" group are instances of low voltages of the QRS complexes in all leads, inversion of the T waves without associated abnormality of the QRS complex, and excessive slurring and notching in unipolar leads. These are nonspecific changes that also are found in the electrocardiograms of patients with severe myocardial failure due to other causes. We believe that they are representative of focal myocardial scarring related to chronic myo-

TABLE 5.—*Postoperative Deaths in Cases of Calcified Aortic Stenosis*

Age, Yr.	Operation	Survival	Grade: Aortic Stenosis	Grade: Coronary Sclerosis	Cause of Death
58	Thyroidectomy	8 days	4	1	Indeterminate; sudden death
62	Gastric resection	2 days	4	1	Shock
64	Pulmonary lobectomy	8 days	2	2	Pulmonary edema
83	Prostatic resection	3 days	3	2	Pulmonary embolus
83	Prostatic resection	3 days	1	3	Shock
59	Cholecystectomy and appendectomy	2 hr.	4	2	Pulmonary edema
61	Cholecystectomy and pyloroplasty	6 days	4	3	Pulmonary edema

7. Dry and Willius.[1] Karsner and Koletsky.[2] Dry, T. J., and Willius, F. A.: Interpretation of the Electrocardiographic Findings in Calcareous Stenosis of the Aortic Valve, Ann. Int. Med. **13**: 143-150 (July) 1939.
8. Dry and Willius.[1] McGinn, S., and White, P. D.: Clinical Observations on Aortic Stenosis, Am. J. M. Sc. **188**: 1-15 (July) 1934.

cardial ischemia and probably poorly understood physiochemical disturbances in the metabolism of cardiac muscle.

As we previously mentioned in the section on myocardial infarction, clear-cut electrocardiographic injury patterns were variable, so that it was difficult to correlate these with clinical myocardial infarction. In some cases the classical changes associated with muscular ischemia and infarction have been obscured by conduction effects and the effects of treatment with digitalis.

TABLE 6.—*Associated Diseases in Forty-Nine Cases of Calcific Aortic Stenosis*

	No. of Cases
Malignant neoplasm	8
Prostatic obstruction	7
Diabetes mellitus	4
Pneumonia	3
Cholecystic disease	3
Gastric ulcer	2
Toxic goiter	2
Chronic leukemia	1
Addison's disease	1
Acute rheumatic fever	1
Bronchiectasis	1
Mesenteric occlusion	1
Gouty arthritis	1
Uremia	1
Fracture of femur	1
Asthma	1

Surgical Experiences.—Statistically significant evaluation of the risk of major surgical procedures on patients with calcific aortic stenosis is not possible from so small a group of patients, particularly since only those persons who have died are included. Nevertheless, we have an impression that surgical procedures are poorly tolerated by such patients, particularly when any degree of postoperative shock results.

Fourteen major surgical procedures involving general or spinal anesthesia were performed at the clinic on 13 of our 49 patients within the five years prior to death. Several others, as well as some of the 13 patients, had had earlier major surgical procedures, and there were also a number of minor operations involving local anesthesia and unaccompanied by significant systemic reaction.

Seven of the 13 patients on whom operations were performed failed to survive the immediate postoperative period. The survival period after operation, the type of operation, pathological findings in the heart, and the cause of death are listed in table 5. It can be appreciated that these patients, all except one of whom had either severe aortic stenosis or coronary atherosclerosis, would tolerate postoperative hypotension poorly without impairment of coronary circulation. Overloading the venous return to the hearts of these patients with parenteral fluid also is hazardous, because of the difficulty of increasing cardiac output through a rigid aortic ostium. This experience must not be interpreted as meaning that the risk of operation is approximately 50%, since many other patients with calcific aortic stenosis have survived operations.

Additional Medical and Surgical Diseases.—It is not surprising to find many medical problems unrelated to the cardiac disease among patients who have calcific aortic stenosis. As was true of our patients, the majority of patients are beyond middle life when the cardiac lesion is recognized and thus are in the age group in which other diseases frequently occur. Unrelated medical and surgical diseases were found in 30 of our 49 patients, and in many cases they were the primary reason that the patient sought medical attention. Ten patients had multiple illnesses in addition to calcific aortic stenosis. The incidence of complicating diseases in the group of 49 patients is given in table 6.

This high incidence of associated diseases is of significance both from the standpoint of the influence of the aortic stenosis on their proper handling and of the influence of these diseases on the heart. We have just stated that in seven cases a fatal outcome followed operation, in which the calcific aortic stenosis undoubtedly had a deleterious effect. The case of Addison's disease may be cited as one in which cardiac decompensation, which led to death, was precipitated by treatment with desoxycorticosterone.

Cause of Death.—Failure of heart and circulation proved to be the immediate cause of death of the majority of these patients, in spite of the high incidence of associated noncardiac disease. Certainly in many instances, however, the noncardiac illnesses were contributory and precipitating factors leading to irreversible myocardial failure. There does not appear to be, however, any significant difference in the survival age of patients with multiple illnesses as contrasted with those with essentially isolated calcific aortic stenosis. The immediate cause of death in our series was determined by careful evaluation of clinical and pathological data (table 7).

COMMENT

An accurate clinical diagnosis of calcific aortic stenosis can be made when all the physical features listed by Christian [9] are present. These include systolic aortic thrill and harsh murmur, often with a softer blowing aortic diastolic murmur; characteristic pulse; decreased or normal pulse pressure; and cardiac enlargement. He also mentioned that the lesion is predominant among older men and that it is slowly progressive, with symptoms of cardiac decompensation appearing late.

TABLE 7.—*Immediate Cause of Death in Cases of Calcific Aortic Stenosis*

	No. of Cases
Myocardial failure	
Chronic congestive failure	18
Acute pulmonary edema	8
Coronary insufficiency	2
Sudden death: undetermined	6 *
Pulmonary embolus	4
Metastatic carcinoma	4
Postoperative shock	2
Bronchopneumonia	2
Acute cholecystitis	1
Intestinal obstruction	1
Barbiturate poisoning	1
Total	49

* Includes two patients who died with convulsive seizures.

Actually, such clear-cut findings cannot always be elicited and the clinician must be satisfied with less evidence on which to base his diagnosis. Roentgenoscopic

9. Christian, H. A.: Aortic Stenosis with Calcification of the Cusps: Distinct Clinical Entity, J. A. M. A. **97**: 158-161 (July 18) 1931.

demonstration of calcification in the aortic leaflets offers positive evidence of the condition and can be relied on if the calcium deposition is sufficient to produce the necessary roentgenologic opacity.

When cardiomegaly is pronounced and myocardial reserve is failing and when emphysematous changes cause separation between the anterior wall of the chest and the heart, the characteristic murmur and thrill may be detected only with difficulty. In such cases, the loudest murmur may be heard at the cardiac apex and cause confusion with mitral valvular disease. The typical cardiac silhouette of left ventricular hypertrophy and evidence of a similar process in the electrocardiogram point toward the aortic stenotic process when the murmur alone is not of diagnostic quality. Treatment of congestive failure with digitalis to improve cardiac output frequently increases the intensity of the basal murmur and brings out the thrill. The detection of calcific aortic stenosis is important not only for the institution of a suitable cardiac regimen but also because the aortic stenosis may influence the choice of therapy and the surgical risk for patients with other medical and surgical problems.

The symptoms of calcific aortic stenosis may be attributed to reduction in cardiac output, as it affects coronary and peripheral circulation, and to failure of the heart as a consequence of the stenotic orifice. We found clinical evidence of coronary insufficiency in 40.8% of our 49 patients. Myocardial ischemia has been shown in some cases to be related to coronary occlusive disease that differs in no way from that seen in patients without aortic stenosis. In dogs with aortic stenosis Green[10] demonstrated decreased coronary blood flow during systole as a result of increased peripheral coronary resistance in relation to aortic pressure. This experimental work offers a well-founded explanation for the angina pectoris of patients who have anatomically good coronary arteries. As the myocardial mass increases with hypertrophy the discrepancy between the available coronary blood flow and the myocardial demand would be accentuated. Other explanations for coronary insufficiency, such as a suction pump effect and obstruction of the aortic orifice with calcification, appear less well founded.[11] Our findings confirm those of earlier studies, i. e., there is an apparent inverse relationship between the severity of the aortic stenosis and the coronary occlusive disease in the majority of patients with calcific aortic stenosis.[12]

Our series has yielded only one proved example of myocardial infarction without significant coronary occlusive atherosclerosis, but this one case confirms another observation that it may occur.[13] In the 49 hearts, we observed the frequent occurrence of small yet macroscopic focal scars, which suggested that rather intense and prolonged ischemia had occurred. This may well explain the discrepancy between the clinical and pathological diagnosis of gross myocardial infarction.

The survival after onset of congestive failure in our group is considerably longer than that reported by Contratto and Levine.[5b] We found an average survival of 2.2 years, which does not support the prevalent conception that congestive heart failure in these patients is usually fulminating. The high incidence of sudden death and acute pulmonary edema has been a factor in this concept. It is our impression that carefully taken histories will reveal failing cardiac reserve and early myocardial failure over a long period in the great majority of patients. Often these elderly persons are incapacitated by other illnesses, so that they do not extend themselves sufficiently to be impressed by their poor cardiac reserve until pulmonary edema makes its dramatic appearance. There is nothing to distinguish the left ventricular failure of aortic stenosis from other processes that cause left ventricular strain.

Further discussion concerning the relationship between congestive heart failure and the anatomicopathological findings are listed briefly in the text of this paper. Why severe myocardial failure develops in some patients who have severe aortic stenosis while others with similar valvular deformity remain compensated is unexplained, just as it is in cases of hypertensive disease.

Longevity is obtained in a large percentage of patients with calcific aortic stenosis. In our series the average age at death was 63.4 years. There were 11 patients whose age at death exceeded 75 years. In this group of 11 patients were three with severe aortic stenosis, five with severe coronary sclerosis, one with both severe aortic stenosis and coronary sclerosis, and only two with mild degrees of both aortic stenosis and coronary sclerosis. Since the valvular deformity was not a recent development in these patients, the immense reserve of the left ventricular myocardium is clearly shown. Such findings do not justify the expression of a pessimistic prognosis to the patient who is given a diagnosis of asymptomatic aortic stenosis in middle life.

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SUMMARY

Forty-nine cases in which calcific aortic stenosis was demonstrated at necropsy were evaluated by correlation of clinical data, electrocardiograms, and necropsy specimens and records. There were 41 (83.7%) men and eight (16.3%) women. The average age at death was 63.4 years, with a range of 39 to 90 years. Angina pectoris occurred in 20 cases (40.8%). Of the patients who had angina, 55% had severe degrees of aortic stenosis and mild coronary sclerosis and 30% had mild aortic stenosis and severe coronary sclerosis. Of the 29 patients who did not have angina, 55.2% had severe aortic stenosis with mild coronary sclerosis and only 6.9% had mild aortic stenosis and severe coronary sclerosis.

The clinical diagnosis of 12 episodes as myocardial infarction was supported by positive pathological findings in only four cases, and the electrocardiogram was diagnostic in only three of these four. This discrepancy has been attributed to the reversible nature of prolonged myocardial ischemia. Myocardial failure occurred in 36

10. Green, H. D.: The Coronary Blood Flow in Aortic Stenosis, in Aortic Insufficiency and in Arteriovenous Fistula, Am. J. Physiol. **115**: 94-103 (March) 1936.

11. Contratto and Levine,[5b] Boas.[6]

12. Dry and Willius,[1] Horan, M. J., Jr., and Barnes, A. R.: Calcareous Aortic Stenosis and Coronary Artery Disease, Am. J. M. Sc. **215**: 451-455 (April) 1948.

13. Friedberg, C. K., and Horn, H.: Acute Myocardial Infarction Not Due to Coronary Artery Occlusion, J. A. M. A. **112**: 1675-1679 (April 29) 1939.

cases (73.5%) and, when it was present, had an average duration of 2.2 years before death. Abnormal electrocardiograms were recorded in 42 of 47 cases. Left ventricular hypertrophy and strain pattern and left bundle branch block were the most frequently observed myocardial injury and conduction disturbances. Auricular fibrillation occurred infrequently.

There were frequent associated but unrelated medical and surgical diseases that were influenced by the heart disease and that influenced the heart disease. In spite of many associated diseases, the terminal event was one of chronic or acute cardiac failure in 28 of the 49 patients. In six additional cases death was sudden and presumably of cardiac origin.

URETHRAL RUPTURE AT APEX OF THE PROSTATE

COMPLICATION OF FRACTURE OF THE PELVIS

John K. Ormond, M.D.
and
P. W. Fairey, M.D., Detroit

Rupture of the urethra at the apex of the prostate is usually seen as one of the less common complications of fracture of the pelvis and therefore may not be cared for in its early stages by a urologist. It is not of frequent occurrence, but the consequences of incomplete, improper, or delayed treatment are so troublesome and incapacitating that its importance is worth emphasizing.

It is most often due to sudden displacement of the bladder and prostate or the triangular ligament, causing rupture of the urethra at its most vulnerable and weakest point. It may be caused by hemorrhage, the accumulated blood pushing the bladder and prostate upward, thus stretching and drawing the membranous urethra out into an unsupported tube, with (frequently) eventual rupture or erosion. It is rarely if ever caused by actual shearing by bone fragments. We have never seen such a case.

It is difficult to conceive of the prostate's being torn from the bladder by trauma, but a consideration of the anatomy of the pelvis will indicate the vulnerability of the junction of the prostatic and membranous urethras (fig. 1). In the performance of radical perineal prostatectomy for early carcinoma, one of the steps is the severance of the urethra at apex of the prostate. No one who has done this can help being impressed by two facts: first, that the apex of the prostate is not bound to the triangular ligament by any strong fibrous structures and, second, that the urethra at this point is relatively unprotected. It is easy to see that, if the prostate were suddenly displaced, laterally, anteriorly, or posteriorly, the membranous urethra, being held almost immovable by the triangular ligament, could be easily torn and that it could easily be drawn upward and eventually torn by movements of the prostate upward. The membranous urethra as it passes through the rather rigid body of the triangular ligament is bound to it by only loose connective and elastic tissue, so that it has a certain amount of freedom of motion longitudinally. It is important that one keep this in mind when performing suprapubic prostatectomy and try to avoid drawing the urethral tube upward and severing it at a low point, for the stump may retract into its path through the triangular ligament and thus lay the groundwork for a stricture.

In every instance of fracture of the pelvis, the condition of the bladder and urethra should be determined as soon as possible. If the patient voids freely and the urine contains no blood, in all probability all is well. However, if there is even a small amount of blood, further diagnostic steps are indicated. In this connection we should like to emphasize the importance of a rectal examination. This should be done in every case, for important information regarding the position of the prostate can be thus obtained.[1]

Fig. 1.—Drawing of perineal exposure of the prostate, showing vulnerability of the junction of the membranous urethra with the prostate. (From Young, H. H., and Davis, D. M.: Practice of Urology, Philadelphia, W. B. Saunders Company, 1926, vol. 2.)

Unfortunately some of the criteria by which the diagnosis of extravasation of urine is usually made are unreliable under the circumstances. Pain, abdominal rigidity, increase in pulse rate, and slight elevation of

From the Henry Ford Hospital.

Read before the Section on Urology at the One-Hundredth Annual Session of the American Medical Association, Atlantic City, June 13, 1951.

1. Culp, O. S.: Treatment of Ruptured Bladder and Urethra: Analysis of 86 Cases of Urinary Extravasation, J. Urol. **48**: 266-286 (Sept.) 1942.

temperature, which are the usual indications of urinary extravasation, may all be present as a result of the general trauma alone.

If the conscious patient is unable to void after a reasonable time, or if there is blood in the urine, catheterization is indicated. The unconscious patient should be catheterized without delay. Sterile water or saline solution may then be injected and withdrawn. If it all returns, rupture of the bladder is improbable, but this test has little value with respect to the urethra.

The only safe and reliable test is the cystourethrogram. Any of the drugs used in intravenous urography may be used as a medium — sodium iodomethamate (neoiopax®), methiodal sodium (skiodan®), iodopyracet (diodrast®), or sodium acetrizoate (urokon®)—or, if these are not available, sodium iodide can always be obtained. Three hundred cubic centimeters of 15% strength can easily be made up. Usually x-ray has to be made with the patient in the supine position only, for the pelvic fracture makes it undesirable to turn him on either side.

When there is complete rupture of the urethra at the apex of the prostate, catheterization is impossible and probably a small amount of blood will issue from the catheter; but, if the rupture is incomplete or if the membranous urethra is drawn upward, the catheter may enter, and the cystogram, as well as the cystourethrogram, may give valuable information, as is shown in one of our cases.

After the diagnosis has been made, the problem of treatment presents itself. There are two objectives: first, as a lifesaving measure, to drain the extravasated urine promptly and with as little disturbance to the patient as possible, and, second, for the sake of the patient's future comfort and efficiency, to reestablish the continuity of the urethra immediately. Of course, the saving of life is most important, but unfortunately the importance of this often looms so great as to obscure the almost equally important consideration of the patient's future well-being.

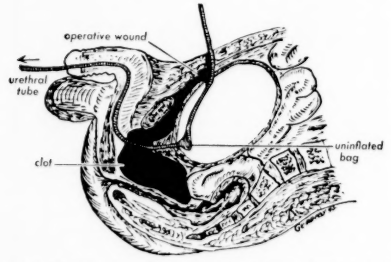

Fig. 2.—Rupture of membranous urethra with blood in the perivesical space. An uninflated Pilcher bag is in place.

In former days there was justifiable reluctance to operate, because operation changes a simple fracture into a compound fracture. However, with the many antiseptic drugs and antibiotics at our disposal now, we need not be afraid of this, and there need be no hesitation about operating. The perineal route gives excellent exposure and makes end to end suture of the urethra easy. However, it is contraindicated under the circumstances and undesirable for other reasons in most instances. It is time consuming and it necessitates flexing the thighs, with

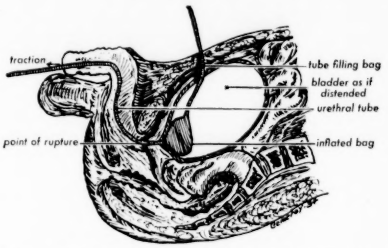

Fig. 3.—Pilcher bag inflated and prostate drawn down into apposition with the membranous urethra.

the further displacement of the fragments of the pelvis, which may cause more soft tissue damage. Furthermore, it is undesirable in young men or boys because possible damage to the nerves of the pelvis may cause impotence, which, indeed, may result from the fracture itself. Moreover, not all surgeons are skilled in perineal surgery.

The easiest, quickest, least traumatizing, and very effective procedure for the accomplishment of both objectives is by the suprapubic route.[2] This permits drainage of extravasated urine and of blood and permits the introduction of catheters or other instruments under the guidance of the eye and hand, by which the continuity of the urethra can be reestablished. It may not be possible to suture the ends together, but, by means of a Pilcher bag or a Foley catheter, traction can be applied in such a way as to keep the severed ends of the urethra in contact until healing takes place. It is not enough merely to introduce a catheter as a splint or guide as is often done. We believe the traction to be an important part of the treatment, for, if healing of the urethra takes place over even a short gap, the groundwork for a stricture is laid.

We advocate that a suprapubic incision be made and the bladder exposed and opened. There will usually be found a mixture of blood and urine deep in the space of Retzius and surrounding the prostate, pushing both bladder and prostate upward. If a Foley catheter is to be used, it can then be passed through the urethra and guided into the bladder by means of a finger or sound thrust into the prostatic urethra through the open bladder; or a sound may be passed and guided in a similar manner, and by means of it, a Pilcher bag introduced. When the bag (Foley or Pilcher) is distended with water, traction will bring the neck of the bladder and the prostate down into apposition with the triangular ligament, and the severed ends of the urethra will be in contact. The whole procedure can be done rapidly and with a minimum of disturbance to the patient. After 10 days or so, the catheter or bag can be removed. After this, sounds should be passed at intervals for a few weeks (fig. 2, 3, and 4).

2. Young, H. H.: Treatment of Complete Rupture of the Posterior Urethra, Recent or Ancient, by Anastomosis, J. Urol. 21: 417-449 (April) 1929.

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This method was first described by Ormond and Cothran in 1934.[3] Since then success by this method has been reported by Rexford,[4] Sewell,[5] Mason and Ratliff,[6] Simpson-Smith,[7] and Reynolds.[8] Leadbetter [9] devised a method by which traction can be applied by means of sutures introduced into the apex of the prostate and brought out through the perineum, and has since sutured the ends of the urethra together through the suprapubic exposure. We believe, however, that the method we describe requires less time and skill and is equally efficacious.

Some of the cases of rupture of the urethra at the apex of the prostate reported herein illustrate the results of this method of treatment, and others, the evil results of neglect, delay, or wrong treatment.

REPORT OF CASES

CASE 1.—The patient as a young boy was run over by an automobile, with a resultant fractured pelvis and ruptured urethra with extravasation of urine. Suprapubic drainage and cystostomy were done, as a lifesaving procedure, but no attention was paid to the urethra. He passed all his urine through the cystostomy for several years. He was then taken to a urologist, who operated by a combined approach, both suprapubic and perineal, and was able to restore the continuity of the urethra. Since 1928 the patient has been under our care and must have the resulting stricture dilated frequently. He has had episodes of infection, and once had to have the bladder opened for a short time. His sexual power is normal. He works and is in good health but as stated above is compelled to have regular (and painful) dilatation of the deep urethra.

CASE 2.—The patient, a 26-year-old man, was admitted a year after the occurrence of a fractured pelvis and ruptured urethra in an automobile accident. There had been numerous operations of various kinds, but, when he was admitted, all the urine came from a suprapubic catheter. By means of a combined suprapubic and perineal operation, we were able to establish urethral continuity. After returning home, he neglected to have dilatations done, and the stricture contracted, epididymitis occurred, and a perineal fistula developed. For 10 years he was in and out of the hospital, and, finally, his ureters were transplanted to the sigmoid.

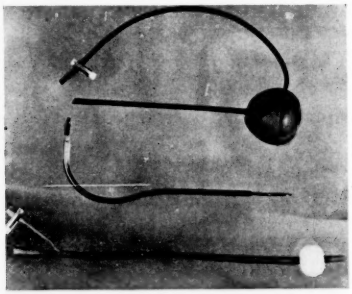

Fig. 4.—From top to bottom, Pilcher bag inflated, sound for inserting Pilcher bag, and 30 cc. Foley catheter, inflated.

CASE 3.—The patient, at the age of 8, in 1942, was hit by a truck, with resultant fracture of both pubic rami and complete severance of the urethra at the apex of the prostate. Suprapubic drainage was established, the perivesical space drained, and a catheter passed into the bladder. No traction was used, and evidently the two ends of the urethra were not brought into close apposition. Healing took place, but a troublesome stricture resulted, which had to be dilated every two months or so, and caused numerous attacks of retention and cystitis. The treatments required anesthesia at frequent intervals, and he had come to dread them greatly. In June, 1950, a combined suprapubic and perineal operation was done. A hard, thick band of fibrous tissue was found and as much as possible excised. He continues to require dilatation, though with much less difficulty than before. His mental condition has benefited greatly, but he will probably require treatment most of his life.

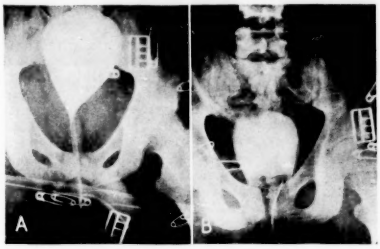

Fig. 5 (Case 6).—Preoperative cystograms. *A*, showing the bladder pushed upward, and *B*, showing the inflated Foley catheter and the bladder pulled down into normal position.

Comment.—Two of these three cases show the results of delaying treatment to the ruptured urethra. In each, drainage of the extravasation was a lifesaving measure, but delay in reestablishing urethral continuity resulted in the necessity for further surgery and in a state of permanent partial invalidism. The other case illustrates the failure of the use of a splinting catheter, without the use of traction. It must be said, however, that successes by this method have been reported.

CASE 4.—This man was caught between the door and the body of his truck when it turned over and was brought to the hospital with bleeding from the urethra, extreme abdominal tenderness, and blood pressure of 60/40. X-rays showed bilateral fracture of both pubic rami. Six hours after the accident, suprapublic incision was made. Complete rupture of the urethra at the apex of the prostate was found. A sound was passed and guided into the bladder and a Pilcher bag introduced by this means. Traction was placed on the bag. Convalescence was uneventful, no stricture formed, and erections were normal.

CASE 5.—The patient, a 37-year-old man, was caught between a crane and a post. Two hours later he was admitted to the hospital, cold and clammy. Blood pressure was 80/40; marked abdominal tenderness was present; and blood was dripping from the urethra. X-rays showed bilateral fracture of both pubic rami. A catheter could be introduced into the bladder. Blood transfusions were given, and a suprapubic incision was made. The urethra was found to be torn away from the apex of the prostate, and a Pilcher bag was used as previously described.

The urethral repair has been satisfactory. The patient has had several attacks of cystitis, and urethral dilatation has been necessary at those times, but he has had no permanent stricture and

3. Ormond, J. K., and Cothran, R. M.: Simple Method of Treating Complete Severance of Urethra Complicating Fracture of Pelvis, J. A. M. A. **102**: 2180-2181 (June 30) 1934.

4. Rexford, W. K.: Rupture of the Bladder and Acute Retention of Urine, Am. J. Surg. **46**: 641-648 (Dec.) 1939; Injuries Involving the Genitourinary Tract, ibid. **74**: 350-358 (Sept.) 1947.

5. Sewell, G.: Personal communication to the authors.

6. Mason, J. T., and Ratliff, R. K.: Urinary Extravasation Proximal to the Triangular Ligament: Method of Repair, U. S. Nav. M. Bull. **49**: 670-680 (July-Aug.) 1949.

7. Simpson-Smith, A.: Traumatic Rupture of the Urethra: Eight Personal Cases, with a Review of 381 Recorded Ruptures, Childbirth and War Injuries Included, Brit. J. Surg. **24**: 309-332 (Oct.) 1936.

8. Reynolds, C. J.: Diagnosis and New Treatment of Traumatic Rupture of Posterior Urethra, South. M. J. **35**: 825-828 (Sept.) 1942.

9. Leadbetter, W. F.: Repair of Complete Tear of the Membranous Urethra: Case Report and Suggested New Technique for Operation, J. Urol. **54**: 549-555 (Dec.) 1945; Personal communication to the authors.

now has not been seen for over two years. He is unfortunately entirely impotent. Nine years ago Lowsley's operation for impotence was performed. At this time the ischiocavernosus muscles were found to be almost completely atrophied.

CASE 6.—The patient, a 20-year-old man, was injured in an industrial accident. An hour later he was admitted to the hospital with blood pressure of 80/50. The catheterized urine was slightly blood tinged. Rectal examination showed the prostate in approximately normal position. X-rays showed fracture of both pubic rami on both sides. A cystogram showed a "tear drop" bladder riding high. Twelve hours later a urethrogram showed extravasation in the region of the posterior urethra. Suprapubic exploration 24 hours after the injury showed the prostate to be completely separated from the membranous urethra. A 30 cc. Foley bag was inserted through the urethra, guided into the bladder, and inflated. Traction was applied (fig. 5). The postoperative course was uneventful. At present, a 24 filiform follower can be passed with ease, and the patient has slight stress incontinence. Erections are reported present.

This case illustrates how misleading simple catheterization can be. The catheter showed no blood, and all the injected fluid was returned. A cystogram showed a "tear drop" bladder riding high, apparently forced up by hemorrhage, and it was not until a urethrogram was made that the injury to the urethra, drawn up as it was, was shown.

Comment.—In the three cases in which traction was used, no permanent stricture has resulted. In one the result was immediate complete restoration to a normal state. In another the state of the urethra is now to all intents and purposes normal. In the third, though the time elapsed since operation has been only a few months, there is every promise that no stricture will result.

SUMMARY

Cases of rupture of the urethra at the apex of the prostate are reported in order to show the vital importance of prompt reestablishment of the continuity of the posterior urethra when rupture of the urethra complicates fracture of the pelvis. A simple and easy method of accomplishing this is described.

SEGMENTAL GASTRIC RESECTION FOR PEPTIC ULCER

METHOD PERMITTING RESTORATION OF ANATOMIC CONTINUITY

Owen H. Wangensteen, M.D., Minneapolis

The evolution of operations for peptic ulcer is an interesting story. Pyloroplasty, gastrojejunostomy, segmental resection for gastric ulcer, antral excision based on elimination of the Edkins factor in gastric secretion, and extension of partial gastric resection to include 75% to 80% of the stomach has been the order of sequence in the development of plastic and excisional techniques in the surgical management of peptic ulcer. There are several variants of these operative procedures, concerned with variations in the technique of their performance, in consequence of which a tremendous literature has been built up around the theme of the surgical management of ulcer. Incomplete vagotomy, an old operation for ulcer employed especially as a complemental procedure to resection, has been revived by Dragstedt and his associates [1] in the nature of complete interruption of vagal influence to the gastrointestinal tract. They, too, however, have found it convenient to add to complete vagotomy a complemental drainage operation, to insure satisfactory gastric emptying.

To operate or not to operate and when to operate for peptic ulcer are still matters concerning which there is no general agreement among leaders in this area of gastroenterological interest. What operation to perform, especially for duodenal ulcer, is a question that elicits many kinds of answers, even from surgeons who profess a special interest in gastric surgery. Even in the matter of how to do the operation, there is no general agreement.

I shall not address myself broadly to all these questions in this presentation. To attempt to do so here would result only in compounding confusion. Up until recently, surgeons seemed generally in agreement on an extensive gastric resection in which the antral mucosa is completely excised, the operation being carried out on the Billroth II plan of operation, with a short, retrocolic duodenojejunal loop employed in effecting gastrointestinal continuity. The only other operation that has had any vogue is the Billroth I gastric resection, in the presence of a suitable duodenum. Then came the worldwide flurry of interest over vagotomy, which has gradually settled back in most areas to a contemplation of regret over the circumstance that so simple an operation as vagotomy should have such serious shortcomings in thwarting the ulcer diathesis. In a few areas, however, there still remains a feverish interest in vagotomy, with the belief that vagotomy continues to be the mainstay of surgical therapy for ulcer. Most surgeons who gave up gastric resection in favor of vagotomy have discarded the latter and returned to use of gastric resection. Even the keen exponents of vagotomy admit that an auxiliary drainage procedure, such as a gastrojejunostomy, is necessary to insure satisfactory gastric emptying after vagotomy. That gastrojejunostomy robs vagotomy of much of its protective action against recurrent ulcer is well documented.[2] Others have complemented gastric resection with vagotomy to augment the protection of resection against recurrent ulcer. We continue to have occasionally echoes of the past in the voices of a few experienced present-day gastric surgeons suggesting that

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1. Dragstedt, L. R.; Harper, P. V., Jr.; Tovee, E. B., and Woodward, E. R.: Section of the Vagus Nerves to the Stomach in the Treatment of Peptic Ulcer, Complications and End Results After 4 Years, Ann. Surg. **126**: 687-699 (Nov.) 1947.

2. Lillehei, C. W., Lewis, J., and Wangensteen, O. H.: The Limitations of a Gastric Drainage Operation upon the Effectiveness of Vagotomy, Gastroenterology **15**: 487-497 (July) 1950.

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gastrojejunostomy,[3] on which I thought funeral obsequies [4] had been conducted years ago, is probably, after all, as good an operation as any for peptic ulcer! These pronouncements serve to remind us that destruction of the Tower of Babel did not end the confusion of voices in many unsettled problems.

It has been proposed many times from this clinic that an operation that will protect against the ulcer provoked in the dog by histamine in beeswax is a good operation for peptic ulcer in man.[5] It is still a good instruction, but many surgeons apparently continue to believe in the empiricism of personal experience and acquaintance with all and any available methods. When will all surgeons manifest that faith in the superiority of experiment over rationalization that every follower of John Hunter professes?

AN OLD PROCEDURE IN MODERN DRESS

I hesitate to advise an operation for peptic ulcer that gastric surgeons cast off long years ago. However, I have put a new dress on this old procedure, and I believe you will find it more acceptable in this new garb. Mikulicz (1897) [6] gave the procedure the name of segmental resection but stated that the results of this operation for ulcer were so poor that he had abandoned the procedure. Riedel (1909, 1912) [7] made the first formal report on use of segmental resection as an operative procedure for gastric ulcer. Payr (1909, 1910),[8] in two papers on the subject, wrote of segmental resection with obvious enthusiasm. The procedure received strong endorsement at the German Surgical Congress in 1912,[9] save for the comment by Marquardt,[9a] who wished at least one instance of its failure to protect against ulcer recurrence recorded.[10] Then, presently, the difficulties with hourglass constriction in the stomach and delayed pyloric emptying dulled the enthusiasm of surgeons for the operation. The last good words spoken for the procedure—and that with some restraint—were by Judd and Lyons [11] at a meeting of the American Surgical Association in 1922. Most of the present generation of surgeons had only heard of segmental resection but had never seen the operation done.

A few years ago I summed up the causes of failure in the difficult technical problem presented by a large supraduodenal ulcer crater and then tried to sketch the outlines of a procedure in which the hazards of the difficult duodenal closure could be circumvented. My first thought was improvement of an earlier technique proposed for excision of the antral mucosa in the pyloric exclusion operation. A simple method of securing hemostasis with a compression ligature, drawn up rather snugly through the eye of a Mayo vein stripper, fitted with an end-plate with two compartments seemed to meet the needs of the situation adequately. Several such operations were done, and rather elaborate sketches were made of the technique. I had fully intended to publish the procedure with the artist's drawings. But amongst those rough sketches made by me to by-pass the perils of a treacherous indurated duodenum were the outlines of the segmental resection I am speaking of here. In the beginning, I believed the operation might find limited usefulness in the simple duodenal ulcer. But as my experience with the method increased it became apparent that this operative procedure was adaptable to the most difficult duodenal ulcer—the circumstance which accounted for my complete loss of interest in the exclusion operation.[12] In other words, experience with segmental resection showed that there no longer seemed to be a necessity for the performance of the exclusion operation. The most difficult duodenal ulcer craters were readily managed by the technique described herein.

Had I been thoroughly familiar with the literature on the abandonment of segmental gastric resection, it is very unlikely that I would have taken up with the method. My belief, of course, was that surgeons had repudiated the operation primarily because it failed to cure ulcer. I surmised that earlier surgeons had not removed enough acid-secreting area. My colleague, Dr. F. John Lewis,[13] has determined the size of the segmental resection in the sketches that Payr [8] used to illustrate the operation in two of his papers on the subject. Save for one instance undertaken for the correction of a gastrojejunal ulcer that gastrojejunostomy, in which 55% of the stomach was excised—as determined from the total surface area—in the remaining illustrations the size of the resection was, respectively, 28.5%, 32%, 39%, and 42.5% of the entire stomach area.

Connell (1929) [14] suggested "fundusectomy" as a likely manner of reducing the acid-secreting area of the stomach, excising a pie-shaped segment with its base at the greater curvatures from the corpus and the fundus. In his sketches shown in the papers of 1929 [14] and 1939,[15] the area of the excised corporic mucosa was, respectively, 22.8%, 34.5%, and 41.4% of the total surface area of the stomach.

3. Walters, W.; Belding, H. H. III, and Lillie, W. I.: Physiological and Clinical Studies of Vagotomized Patients: A Study of 331 Patients, Arch. Surg. **62**: 183-205 (Feb.) 1951.

4. Wangensteen, O. H.: The Passing of Gastrojejunostomy as a Standard Operation for Ulcer, Journal Lancet **62**: 415, 1942.

5. Lannin, B. G.; Hay, L. J.; Judd, E. S., and Wangensteen, O. H.: Evaluation of a Satisfactory Operation for Ulcer, Proc. Soc. Exper. Biol. & Med. **56**: 231-233, 1944. Lannin, B. G.: Experimental Evaluation of a Satisfactory Operation for Ulcer, Surgery **17**: 712-741, 1945.

6. Mikulicz-Radecki, J.: Die chirurgische Behandlung des chronischen Magengeschwürs, Verhandl. d. Deutsch. Gesellsch. f. Chir. **26**: 31, 1897.

7. Riedel, B.: Die Entfernung des mittleren Abschnittes vom Magen wegen Geschwür., Deutsche med. Wchnschr. **35**: 17, 54, 1909; Das jetzige Verhalten von 18 wegen Ulcus curvat. min. mit Entfernung des mittleren Theiles vom Magen behandelten Kranken, Verhandl. d. deutsch. Gesellsch. f. Chir. **41** (pt 2): 61-75, 1912.

8. Payr, E.: Erfahrungen über Excision und Resection bei Magengeschwüren, Arch. f. klin. Chir. **90**: 989, 1909; Erfahrungen über Excision und Resection bei Magengeschwüren, ibid. **92**: 199, 1910.

9. In discussion of Reidel, B.: Verhandl. d. deutsch. Gesellsch. f. Chir. **41**(pt. 1): 162-176, 1912; (*a*) Marquardt, p. 175; (*b*) A. Bier, p. 173; (*c*) H. Kummel, p. 170; (*d*) E. Payr, p. 162.

10. In his second paper on segmental gastric resection for ulcer, presented before the German Surgical Congress in 1912, Riedel, of Jena, stated that he had done the first operation of this type on July 10, 1901, and the second on Aug. 18, 1905. Bier,[9b] of Berlin, in the same discussion stated that he had performed segmental resection for gastric ulcer successfully in one patient 13 years previously and in another 10 years previously. Kummell,[9c] of Hamburg, stated that he had performed segmental gastric resection for cancer 16 years before. Payr,[9d] though extolling segmental gastric resection as the best operation for ulcer of the body of the stomach, stated that Hoffman (1906) of Kummell's Clinic, Mikulicz (1897), and others had observed recurrences after segmental resection for gastric ulcer.

11. Judd, E. S., and Lyons, J. H.: Resection of the Body of the Stomach for Ulcer: Report of a Series of Cases with End Results, Ann. Surg. **76**: 409-420, 1922.

12. Wangensteen, O. H.: Method of Closing the Pyloroantral Pouch in the Antral Exclusion Operation, Surgery **12**: 731-741, 1942.

13. Lewis, F. J.: Personal communication to the author, 1951.

14. Connell, F. G.: Fundusectomy; New Principle in Treatment of Gastric or Duodenal Ulcer, Surg., Gynec. & Obst. **49**: 696-701, 1929.

15. Connell, F. G.: Problem of Intractable Peptic Ulcer, Surg., Gynec. & Obst. **69**: 287-290, 1939.

In 1940,[16] I suggested a modification of Connell's procedure, in which the entire greater curvature from the area immediately to the left of the esophagus to the antrum was excised, converting this segment into a tube. Assessment of the extent of the resection by the surface area method in figure 13 of that paper, employed to illustrate the technique, suggests that 55% of the entire stomach and 68% of the acid-secreting area was excised. I did five such operations; two of the patients had recurrent duodenal ulcers within a few years, necessitating re-resection by the conventional Billroth II method. Eight such tubular resections were performed with simultaneous complemental gastrojejunostomy.

It is clear from these computations of the surface area that, in Payr's segmental resections, in Connell's fundusectomy, and in my tubular resection, that not enough of the acid-secreting area was removed to protect against recurrent ulcer.

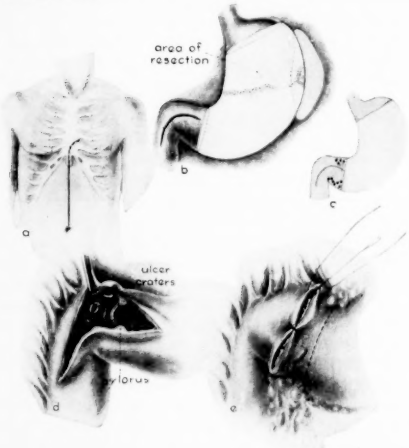

Fig. 1.—*a*, Sternotomy incision. *b*, The area of stomach to be excised. The shaded areas show the size of the residual fundic pouch and the pylorotomy incision. The light area to be excised is 80% of the entire stomach and 90% of the acid-secreting area. *c*, The maximal count of parietal cells is in the light area; in the shaded fundic zone the parietal cell count per unit of area is less; moreover, studies on isolated pouches in the dog show there is less acid secreted there per unit of area than in the corporic light zone; there are very few parietal cells in the antrum. *d*, Two ulcer craters are shown just beyond the pylorus; the long duodenoantral slit affords good visualization of the entire pyloric region. *e*, The closure of the pylorotomy incision. There are two rows of sutures. The site of application of the clamp for the distal line of resection also is sketched in.

In the revival and revision of segmental resection, I proposed preserving the pylorus and the entire antrum intact, removing the greater portion of the acid-secreting area and leaving only a small residual gastric pouch beyond the esophagus, constituting less than 10% and somewhat more than 5% of the entire stomach area. That such an operation protected against ulcer provoked by histamine in beeswax in dogs was readily ascertained, a circumstance which augured well for the ulcer-thwarting properties of the procedure. The first four patients subjected to the operation had duodenal ulcers without too much deformity of the duodenum. All these patients exhibited difficulty with gastric emptying after the operation. In the first patient, no operation was done on the pylorus. Bethanechol (urecholine®) chloride was given; the motility of her stomach improved gradually, and she weathered the inconvenience of gastric retention satisfactorily. In the next two patients, an extramucosal pyloromyotomy of the Ramstedt type was done; in the succeeding two patients, the incision was extended through the mucosa, with a longitudinal serosal closure. Even this was not enough to insure entirely satisfactory emptying of the stomach, and I began making a very long duodenoantral slit, 8 to 12 cm. in length, taking great care to observe that the incision was long enough to have divided any areas of constriction or narrowing in either the duodenum or the antrum. This rather long slit was then closed transversely. None of these patients have had any difficulty with gastric emptying, which enabled me to persuade patients who still had some gastric retention to submit to a secondary pyloroplasty on the duodenoantral segment of their stomachs.

In retrospect, it was readily appreciated that excision of a wide gastric segment had deprived the pylorus and the antral gastric fragment of its vagus nerve supply, an occurrence that neither earlier segmental resectionists nor I had taken into account. Moreover, they had used the method only for gastric ulcer; I was employing it in patients with duodenal deformities. Making a long duodenoantral slit, which when closed transversely provided a lumen as wide as the normal duodenum, resolved not only the riddle of the pyloric obstruction attending segmental resection but solved other aspects of the problem as well.

TECHNIQUE

1. *Incision.*—Figures 1 and 2 illustrate very nicely the technique of the procedure. A midline supraumbilical incision, extending to the xiphoid, suffices in thin patients. The majority of patients who come to operation for ulcer, however, have grown large around the waist, while trying to eat their way out of the difficulties of peptic ulcer. To get satisfactory exposure of the subdiaphragmatic esophagus and gastric fundus, I have added a median extrapleural sternotomy.[17] It affords easy and direct access to the attic of the abdomen. Sternotomy is simply and quickly done with a Lebsche sternum knife; it is as easily closed. In making the incision, one should be careful not to injure the pleura as the knife cuts out into the fourth and fifth interspace (fig. 1*a*).

The sternum is rewired with the placement of a few steel wires (no. 24). In men, in whom the sternum is usually wide, a few drill holes are placed; in women, in whom the gladiolus of the sternum is frequently narrow, these wire sutures may be placed about the sternal fragments with a Mayo type fascia needle. It has been gratifying to note the excellent exposure sternotomy affords and how little disability it provokes. Combined with a midline supraumbilical incision, it has come to be the incision of choice in the University of Minnesota clinic in operations on the stomach, liver, diaphragm, and spleen.

2. *Duodenoantral Slit.*—The lateral avascular ligament of the duodenum is divided. The duodenum and antrum are drawn into the operative field, and a longitudinal slit is made through the pylorus and is extended well into the duodenum and the antrum. At this juncture, I insert a curved, blunt-nosed hemostat into the

16. Wangensteen, O. H.: Aseptic Gastric Resection; a Method of Aseptic Anastomosis Adaptable to Any Segment of the Alimentary Canal (Esophagus, Stomach, Small or Large Intestine); Including Preliminary Description of Subtotal Excision of the Acid-Secreting Area for Ulcer, Surg., Gynec. and Obst. **70**: 59-72, 1940.

17. Wangensteen, O. H.: An Assessment of Etiologic Aspects of Peptic Ulcer and Surgical Therapy, Including Obscure Massive Acid-Peptic Linked Hemorrhage, Esophagitis and Cardiospasm and Their Surgical Relief (The Alvarenza Lecture IX), Tr. & Stud., Coll. Physicians, Philadelphia **18**: 1-16, 1950.

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duodenum and the antrum, to be certain that no areas of narrowing remain. An incision 8 to 10 cm. in length is usual; if there is considerable scarring or narrowing, I do not hesitate to make the incision longer.

Surgeons as well as roentgenologists are intrigued by the findings that this long slit uncovers. Both have learned how important it is to restudy their x-rays with greater care for evidences of small defects. In addition to a large ulcer crater or two, there may be several small superficial ulcers; this circumstance has been observed repeatedly.

Closure of the incision is begun by approximating the two far points of the incision. It is surprising how easily this long slit comes together for closure in the transverse direction (fig. 1*e*). A few mucosal stitches of fine silk (00000) are placed first, and then another inverting row of interrupted silk stitches (0000) is placed to complete the closure. If there is a large supraduodenal ulcer crater, the surgeon must place the three or four stitches at the upper end with studied care, to make certain that the closure is satisfactory. While doing so, he cannot help being reminded how very much simpler the task is than if he were attempting to effect an inversion of such a duodenum with the Billroth II type of operation (fig. 1*d* and 1*e*).

3. *Resection.*—The size of the excised fragment of the stomach is indicated in figure 1*b*. Surgeons have learned that, when the antrum is removed completely, 75% to 80% of the stomach has to be removed to insure protection against recurrent ulcer. Obviously, therefore, when the antrum is left, a larger segment must be removed. It has been my practice to leave only enough gastric fundus to make it possible to effect the anastomosis with the antrum satisfactorily. Such a fragment represents approximately 5% to 10% of the entire stomach and less than 15% of the acid-secreting area of the stomach (fig. 1*b*). In patients, as well as in dogs subjected to the histamine-in-beeswax test of the protective action of this operation against recurrent ulcer, this extent of resection appears to afford satisfactory protection against recurrent ulcer. The virtue of the histamine assay is that it assesses the merit or weakness of any proposed operation directly and quickly. Nevertheless, it will be important to know, too, whether a five-year follow-up on patients subjected to this extent of resection will verify the impression that these patients will receive absolute protection against recurrent ulcer. In the experience at this clinic, the histamine test has proved an excellent criterion for predicting the promise or detecting the defects of any operation proposed to thwart the ulcer diathesis.

Inasmuch as only the small upper fundic fragment remains "unvagotomized" by this operation, complemental division of the vagi trunk on the esophagus has been done latterly in a few patients, leaving regularly a 10% fundic pouch. With the use of the histamine test in dogs, an attempt has been made to determine how much larger, if any, the upper fundic pouch may be when the vagal trunks are divided. Those experiments indicate clearly that complemental vagotomy does not make it safe to leave a 25% residual fundic pouch when doing a segmental resection.[18] In fact, it would appear to be the better part of wisdom, as far as recurrent ulcer is concerned, not to expect too much from a complemental vagotomy on the residual fundic pouch.

4. *Anastomosis.*—The first trials with a closed type of gastric resection were made in this clinic early in 1938; by 1940, the closed anastomosis had been adopted by all our surgeons and has continued to be standard practice [19] for gastric resection in the Billroth I and II type of operation in this clinic.

Surgeons who employed segmental resection for gastric ulcer or cancer 30 years or more ago renounced the operation, in part because of the development of an hour-glass constriction at the site of suture. This phenomenon was observed also in two of my earlier patients who were subjected to reoperation. Because of this occurrence, and because the pyloroplasty is an open operation anyway, I now make the anastomosis between the antrum and the small upper residual gastric fragment by a combination of the closed and the open methods. I feel that the corners are turned in more readily by use of the closed anastomosis. A row of interrupted silk sutures is placed behind and tied. The clamps are turned over and the corner angles are dealt with by the placement of two sutures anteriorly at either end of the anastomosis, which are tied after the clamps are withdrawn (fig. 2*g*). This maneuver permits inspection of the interior of the anastomosis and the placement of a few stitches to insure satisfactory mucosal apposition. At this juncture, the in-lying gastric tube, which was pulled back by the anesthetist into the distal end of the esophagus as the anastomosis was started, is grasped and is threaded through the pyloroplasty into the duodenum. A few mucosal stitches of fine silk are placed anteriorly, and another row of sutures in the serosa completes the anastomosis anteriorly. The end stitch at the lesser curvature, which has been left long, is now pulled behind the anastomosis, and the posterior suture is rotated to bring the serosal surface into direct view, permitting placement of an additional stitch between each of the posterior row of stitches placed at the beginning of the anastomosis (fig. 2*k*).

Three or four stitches are employed to fasten the lesser curvature of the stomach to the hepatoduodenal ligament beneath the liver (fig. 2*l*). The greater omentum is removed routinely in the early part of the dissection. The colon is not fastened back to the greater curvature of the miniature stomach.

For several years I have been removing the spleen regularly in all patients operated on for peptic ulcer who give a history

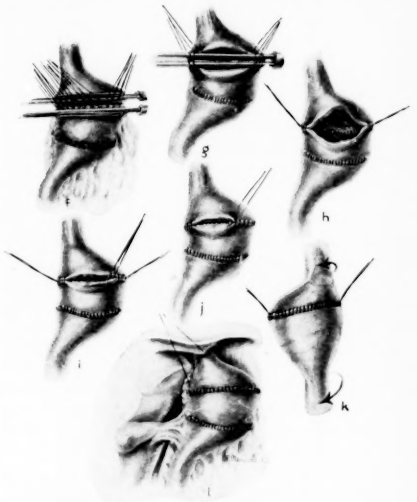

Fig. 2.—*f*, The beginning of the anastomosis following completion of the excision of gastric tissue. *g*, The clamps have been reversed and the two corner stitches at each end are placed. *h*, The pouch has been opened and a few mucosal stitches are placed. At this juncture, the indwelling duodenal tube, which during the operation was pulled back into the esophagus, is now pushed through the pyloroplasty well into the duodenum. *i* and *j*, Completion of the anterior row. *k*, Rotation of the anastomosis to permit placement of a few additional interrupted silk sutures in the posterior row, from the outside. *l*, The completed anastomosis. The lesser curvature is attached by a few sutures to the hepatic margin of the hepato-duodenal ligament.

of hemorrhage, for it has seemed to me that there is an accompanying element of purpura in some of these hemorrhages. Moreover, in two women operated on by me several years ago for bleeding duodenal ulcer, in whom the spleen was not removed, cutaneous petechial hemorrhages as well as other evidences of mild purpura have been observed since.

Early in the dissection, great care is observed to preserve the vessels along both the lesser and greater curvatures of the antrum. In the upper segment, the lesser and greater curvatures are

18. Cross, F. S.; Ferguson, D. J., and Wangensteen, O. H.: Evaluation of Segmental Gastric Resection for Peptic Ulcer, Proc. Soc. Exper. Biol. & Med. **77**: 689-692, 1951.

19. Wangensteen, O. H.: Aseptic Resections in the Gastro-Intestinal Tract with Special Reference to Resection of the Stomach and Colon, Surg., Gynec. & Obst. **72**: 257-281, 1941.

mobilized completely, severing any vessels along their margins. The only remaining blood vessels to the tiny residual upper segment are one or two vessels on the posterior wall. On a few occasions, when leaving only a 5% upper residual pouch, I have found that detachment of all the blood vessels along the curvatures left the remaining upper gastric fragment without any blood vessels, save for those coming down through the esophagus. In such instances, no suggestion of an inadequate blood supply to the tiny residual upper gastric fragment has been noted and no difficulty on this score has been encountered in the postoperative period.

RATIONALE OF THE OPERATION

The antrum itself secretes very little acid, a fact that was established by Heidenhain [20] by the employment of isolated gastric pouches in the dog, before histological verification of the function of the parietal cells by Bensley (1898).[21] Ivy and Oyama [22] failed to find acid or pepsin secretion in isolated antral pouches. With respect to the operation proposed herein, granted only a small area of acid-secreting area remains (responsive area), what harm can it do to leave the gastrin-containing antrum (effectuator area), in which little if any hydrochloric acid is secreted? In fact, I am inclined to believe that surgeons have persisted in performing the operation in the conventional manner largely because it is the easiest method by which to reduce the size of the stomach.[22a]

INDICATIONS AND CONTRAINDICATIONS

The sole contraindication for the procedure so far encountered has been the presence of an antral ulcer. Obviously such an ulcer should always be excised, lest an occult gastric cancer be overlooked. The most difficult duodenal ulcers with considerable induration, including large supraduodenal craters, have been operated on by this technique. A stenotic duodenum is not a contraindication to employment of the method. A long incision carried well into the antrum, as well as into the duodenum, and closed transversely affords adequate promise that obstruction will not ensue. The operation has been undertaken several times during the course of active massive hemorrhage. One of the distinct advantages of the procedure in bleeding duodenal ulcers is that the bleeding point can be visualized and dealt with directly. The operation has been done for idiopathic stricture of the esophagus, which is manifested by the regurgitation of acid-peptic juice into the esophagus. The operation has been performed in one patient in whom the distal half of the esophagus was almost completely stenosed, after the ingestion of concentrated hydrochloric acid with suicidal intent. Whereas initially the patient had difficulty with swallowing water, he now can eat a balanced meal. Since performance of the segmental resection, this patient's esophagus will admit a no. 30 (F) bougie. Prior to operation, it was impossible to introduce a catheter into the strictured esophagus. Recent experimental studies have shown the great vulnerability of the esophagus to injury by acid-peptic juice as well as by bile and pancreatic juice. In patients with defects at the upper portion of the lesser curvature in whom segmental resection is contemplated, but the finding of a suspicious lesion dictates the wisdom of excising all the fundic mucosa together with a few centimeters of the esophagus, I prefer to perform a Ramstedt extramucosal myotomy on the pylorus rather than a Heinecke-Mikulicz pyloroplasty. This is understandable, for the loss of the normal anatomic esophagogastric juncture in the presence of a pyloroplasty is likely to invite regurgitation of bile into the esophagus. This same course of action is advisable when the hypertonic distal esophagus together with the acid-secreting area of the stomach is excised in the surgical correction of megaesophagus.[23]

The lessons of the clinic [24] and the experimental laboratory [25] with reference to the vulnerability of the esophagus to injury by bile and pancreatic juice are impressive. In fact, esophagitis leading to severe anemia can be produced in the dog by the migration of the bile and pancreatic juice containing duodenal segment up onto the lower thoracic esophagus.[26] This esophagitis is observed, too, when the stomach is excised. A bit of gastric mucosa, the size of a penny, when swung up onto the esophagus on a vascularized pedicle, will cause an acid-peptic ulcer in the esophagus, even when the remainder of the stomach is excised.[27] This circumstance suggests the clinicians need to re-alert themselves to the great susceptibility of the esophagus to injury by chemical agents. Finally, segmental resection has added strong confirmation to the thesis that excision of the ulcer is not necessary to cure the ulcer diathesis, as some surgeons have continued to insist.

RESULTS

Sixty patients have been operated on by this method in the past two years at the Minnesota University Hospital. There has been one hospital death in the series. The patient had an intrahepatic gallbladder that was excised at the same time as the stomach segment; the patient died of biliary peritonitis, despite the presence of in-lying drains, a week after the operation. Plans had been made to do a "suction tip" exploration (fig. 3); however, because of the rather free external drainage of bile, it was not undertaken.[28] Autopsy disclosed a good deal of bile in the peritoneal cavity. There has been one additional early death in the series, the patient dying of encephalitis several months after operation.

20. Heidenhain, R.: Untersuchungen über den Bau der Labdrüsen, Arch. f. mikr. Anat. **6**: 368, 1870.

21. Bensley, R. R.: The Structure of the Mammalian Gastric Glands, Quart. J. Micr. Sc. **41**: 361, 1898.

22. Ivy, A. C., and Oyama, Y.: Secretion of the Pars Pylorica Gastri, Am. J. Physiol. **57**: 51, 1921.

22a. The manner in which the remaining antrum invites recurrent ulcer in the conventional Billroth II operation is a question of perennial interest to surgeons. Every surgeon knows that the Eiselberg (Arch. f. klin. chir. **50**: 919, 1895) pyloric exclusion operation as well as the operation of Devine (Surg., Gynec. & Obst. **47**: 239, 1928) invite ulcer recurrence. When considering that retention of the antrum is not followed by recurrent ulcer in segmental resection performed as described herein, it becomes clear that it is separation of the antrum from the residual stomach that predisposes to recurrent ulcer. This thesis is supported too in the observations of Koennecke (Arch. f. klin. chir. **120**:537, 1922) on migration of the antrum to the terminal ileum as well as in the recent experiments of Dragstedt, Oberhelman, and Smith (A. M. A. Arch. Surg **63**: 298 [Sept.] 1951).

23. Wangensteen, O. H.: A Physiologic Operation for Mega-Esophagus: (Dystonia, Cardiospasm, Achalasia), Ann. Surg. **134**: 301, 1951.

24. Wangensteen, O. H., and Leven, N. L.: Gastric Resection for Esophagitis and Stricture of Acid-Peptic Origin, Surg., Gynec. & Obst. **88**: 560-570, 1949.

25. Ferguson, D. J., and others: Studies on Experimental Esophagitis, Surgery **28**: 1022-1039, 1950.

26. Cross, F. S., and Wangensteen, O. H.: The Role of Bile and Pancreatic Juice in the Production of Esophageal Erosions and Anemia, Proc. Soc. Exper. Biol. & Med. **77**: 862-866, 1951.

27. Arroyave, R.; Clatworthy, H. W., and Wangensteen, O. H.: Experimental Production of Esophagitis and Esophageal Ulcers in Dogs, Surg. Forum **1**: 57-59, 1950.

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It is somewhat early to discuss the results of segmental resection for ulcer. However, a study of these patients suggests definitely that achlorhydria to histamine is about as common (65% of instances), as it is after the three-quarter gastric resection by the Billroth II method. However, it should be remarked that this finding is probably more significant in these patients, in that the stomach does not empty so readily as it does after the conventional Billroth II operation. Whereas patients who ingest 5 oz. (150 cc.) of barium with that type of procedure frequently have empty stomachs within 10 minutes (contrasted with some evidence of barium retention within a normal stomach after 80 minutes), after the type of operation described herein, ingestion of the same amount of barium is retained within the stomach approximately 30 minutes or more. Pylorotomy, of course, robs the patient of the type of reservoir he had prior to the operation. Yet, in time, a small miniature stomach, which serves the function of a reservoir, appears to develop.

It had been my hope initially that this procedure might do away completely with the so-called dumping syndrome, which occurs rather frequently after the Billroth II operation. Whereas my results in this respect were somewhat better than were observed in the patients subjected to the Billroth II operation, nevertheless, sweating, fulness, and some qualitative food distress are observed in the early convalescence after this operation.

As a group, these patients do not seem to lose as much weight as do the patients who have undergone the conventional Billroth II type of operation for ulcer. Absorption studies of ingested fat suggest that, on the whole, not as much fat is lost in the stool as after the conventional Billroth II operation for peptic ulcer.

It is much too early to speak of definitive results. However, in patients operated on more than a year ago, it would appear that the excellent and good results are at least as frequent as they are after the Billroth II operation.[29] Only time will tell whether this procedure will come to supplant the conventional three-quarter gastric resection for peptic ulcer. No recurrences have been observed during this brief period of follow-up. Moreover, the histamine-in-beeswax studies on dogs suggests that the ulcer diathesis should be adequately dealt with by the use of the operation described herein. It is obvious that this operation can be done under circumstances that would make it impossible to do the Billroth I operation; moreover, the pyloric sphincter is completely lost in the Billroth I operation. That the pathway of the food is in a natural direction is, of course, a great gain of the operation over the conventional Billroth II operation. It is to be expected, therefore, when a review is made of a group of patients operated on three to five years previously, that the patients will be lean after segmental gastric resection probably less frequently than after the Billroth II type of procedure. Moreover, if current observations are borne out, the "dumping syndrome" will constitute less of a problem than it appears to be after the Billroth II operation. Unlike the Billroth II procedure, after which sideropenic anemias, usually mild, are rather frequent, anemia has not been observed after the segmental resection.[30] Whether this occurrence is due to maintenance of the antrum or to preservation of the normal mode of entry of the digestive secretions into the alimentary tract remains to be determined. Bohmansson (1950)[31] has pointed out that, in this respect, the Billroth I procedure is also functionally superior to the Billroth II operation.

SUMMARY

A segmental resection in which the antrum is allowed to remain and a small segment of the fundus beyond the esophagus, constituting not more than 10% of the entire stomach or 15% of the acid-secreting area, is preserved, when accompanied by an adequate pyloroplasty, is a satisfactory operation for ulcer. Such a procedure will protect the dog against the ulcer provoked by histamine in beeswax. This operation may be performed for duodenal as well as gastric ulcers located in the stomach proximal to the antrum. The procedure is particularly adaptable to large and difficult supraduodenal ulcer craters in which performance of the Billroth I procedure is not possible and in which the Billroth II operation would carry considerable hazard. Moreover, the procedure is the operation of choice in bleeding duodenal ulcers, because of the ease of dealing with the site of hemorrhage. Whether segmental resection will come to supplant the conventional Billroth I and II operations when any one of the three procedures may be done, only time will tell.

Segmental resection as described herein appears to thwart the ulcer diathesis in both dog and man. When accompanied by a sternotomy incision, it is easily performed. The early results of the operation appear to compare favorably with the results of the more conventional modes of gastric resection.

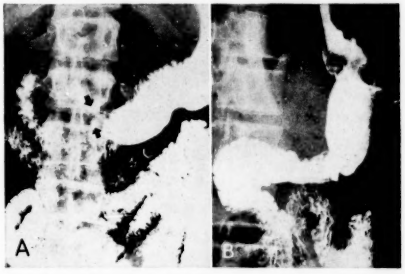

Fig. 3.—*A*, before operation. The two ulcer craters designated by the arrows were identified at operation. *B*, after operation. A little more antrum remains than is conventional. (Compare with sketches in figure 2.) The ulcer craters are healed. The patient has done very well.

28. Surgeons should do these "suction tip" explorations (Wangensteen, O. H.: Problems of Acute Intestinal Obstruction, Rev. Gastroenterol. **17**: 756-780, 1950) of the abdomen on lesser indications than we are accustomed to employ in patients who are not doing well after abdominal operations. It has been used over a period of three years in this clinic. It is, I believe, a useful method to detect the presence of an occult subphrenic, subhepatic, or lateral gutter abscess. In this clinic it has been the agency of saving lives. But even we, as the instance of the patient cited above suggests, do not use the method as often as we should. The method is deserving of trial, I believe, in the recognition of strangulating obstructions, pancreatic necrosis, and related conditions in which an accurate diagnosis is important and difficult to make. Moreover, in the removal of an intrahepatic gallbladder, it is always wise to insert a T tube into the common bile duct, and the employment of irrigation will help to detect a leak in the liver substance.

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SURGICAL ASPECTS OF HYPERSPLENISM

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and
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Certain blood dyscrasias due to splenic disease that may be amendable to splenectomy have been delineated by the hematologists. Surgery is frequently recommended in these cases, despite alarming deficiencies of blood cells or platelets that cannot be replenished to the commonly accepted safe preoperative levels. A satisfactory outcome, however, is possible if the diagnosis is confirmed by a competent hematologist and a few details of preoperative care are followed by a painstaking technique in splenectomy.

Since the surgical aspects of hypersplenism often depend on the type of blood dyscrasia, the surgeon must have a basic understanding of these disease entities in order to work effectively with the hematologist in planning the surgery as well as the preoperative and postoperative care. It is not our intention to discuss the diagnostic and prognostic aspects of hypersplenism, but it

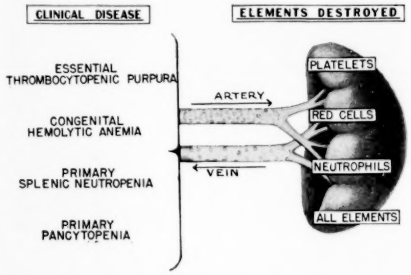

Fig. 1.—Schematic representation of one mechanism of hypersplenism (primary). The clinical syndrome is dependent on the blood element or elements destroyed.

will be necessary to define the various types, as they may present problems in their individual surgical management.

The syndrome of hypersplenism denotes an increase in the breakdown of one or more elements of the blood by the spleen.[1] The exact mechanism of hypersplenism is debatable and is under considerable investigation by hematologists.[2] Regardless of the mechanism, specific disease entities are recognized dependent on the deficiency of the blood element or elements. Furthermore, these disease processes are classified as primary hypersplenism if congenital or hereditary and as secondary hypersplenism if they occur as a complication of a chronic disease.

In primary hypersplenism, platelets, red blood cells, or neutrophils, or all three of these elements of the blood, may be destroyed by the spleen (fig. 1). As a result, four clinical diseases are recognized. Excessive destruction of platelets results in essential thrombocytopenic purpura. The destruction of red cells in primary hypersplenism produces congenital hemolytic anemia. The more recently recognized syndrome of primary splenic neutropenia is a consequence of increased destruction of the neutrophils.[3] If all three of these elements are deficient as a result of hypersplenism, the clinical disease is known as primary pancytopenia.[4] Splenectomy in this group of diseases will usually effect a cure of the primary hypersplenic syndrome.

Secondary hypersplenism produces a clinical picture identical with that of primary hypersplenism but occurs as a complication of a number of chronic disease processes, such as chronic leukemia, Banti's disease, Boeck's sarcoid, Hodgkin's disease, and certain infections (fig. 2). For convenience we have included two more disease entities, acquired hemolytic anemia and neutropenia of Felty's syndrome, a secondary hypersplenism, although it is realized that there is no known associated complicating disease. The astute hematologist has found that, during an unsatisfactory phase of one of the above-mentioned generalized systemic diseases, there may be a superimposed overactivity of the spleen, producing secondary thrombocytopenic pupura, secondary hemolytic anemia, secondary splenic neutropenia, or secondary pancytopenia. The spleen has been proved the offending factor in the production of these cytopenias, and this phenomenon is described as secondary hypersplenism. Splenectomy may prolong life in the patient with secondary hypersplenism or establish a more favorable hematologic state; however, it will not alter appreciably the eventual outcome of the primary disease.

In the general surgical service of the University Hospital, there were 144 consecutive patients exhibiting primary or secondary hypersplenism referred by the department of hematology for splenectomy during the period April 1, 1946, to Jan. 1, 1951. There were 90 patients with primary hypersplenism and 54 patients with secondary hypersplenism. Further subdivision of the disease entities in primary hypersplenism and secondary hypersplenism is given in figure 3. Although essential thrombocytopenic purpura was seen in 55% of the cases of primary hypersplenism, thrombocytopenia was seen in only 13% of the cases of secondary hypersplenism. Hemolytic anemia was present in 30% of the primary cases and 42% of the secondary cases of hyper-

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splenism. The increased incidence of neutropenia in secondary hypersplenism (37%), as compared with primary splenic neutropenia (10%), was accounted for in large part by a number of cases of Banti's disease, though only those in which hypersplenism was exhibited are included. The relative frequency of pancytopenia in the two groups is similar.

The absolute prerequisite for good results of splenectomy in the hypersplenic state is the preoperative confirmation of the diagnosis. Although peripheral blood cell counts may be suggestive, bone marrow studies must be made by a competent hematologist to establish the diagnosis of hypersplenism. Caution must be exercised in the differential diagnosis, since bone marrow replacement, toxic drugs, and frequently seen industrial toxins may produce a peripheral blood pattern similar to that of hypersplenism. In hypersplenism, bone marrow hyperplasia for the specific cytopenia is always present. Further confirmation of the spleen as the etiological factor in the production of a specific cytopenia may be obtained with the epinephrine test. The diagnosis was established in each case by the hematology department prior to the recommendation for splenectomy.

Adjunct liver function studies were usually made and often were of paramount prognostic significance in cases

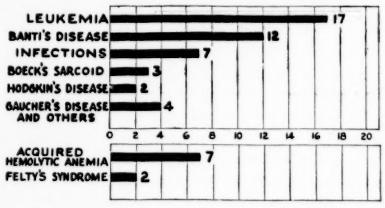

Fig. 2.—The diseases in which splenectomy was performed for associated secondary hypersplenism. Acquired hemolytic anemia and Felty's syndrome are included, although no primary associated disease is known.

of secondary hypersplenism. These tests included determinations of the total protein and albumin-globulin ratio, prothrombin time, serum bilirubin, alkaline phosphatase, thymol turbidity, and cephalin flocculation. Failure of prothrombin time to rise above 50% with adequate vitamin K therapy usually denotes liver involvement by a primary chronic disease process and has been found to signify a poor prognosis. Renal function studies and determinations of the cardiac and pulmonary status were made when indicated.

PREOPERATIVE CONSIDERATIONS

The hypersplenic patient usually confronts the surgeon as a problem in preoperative management. In primary hypersplenism the patients are usually young; they averaged 22.5 years in our 90 consecutive cases. Their average vital capacity was 3,200. There was no associated debilitating disease. However, severe anemia was present in 20% of the patients at the time of operation. In contrast, the surgical risk in secondary hypersplenic patients is much greater. The vital capacity in 54 consecutive cases averaged only 2,400, and 93% had an associated debilitating disease. Sixty-seven per cent of these patients had severe anemia at the time of splenectomy. Although the average age was 30.8 years, this is readily explained by the inclusion of a number of younger patients with Banti's disease in this particular group. When the patients with Banti's disease were excluded, the average age of the remaining patients was 44 years, or twice that of patients with primary hypersplen-

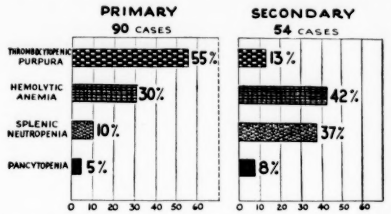

Fig. 3.—The comparative incidence of the cytopenias seen in 90 cases of primary and 54 cases of secondary hypersplenism.

ism. In general, therefore, there was a marked difference in the general condition of the two groups of hypersplenism, since so many of the patients in the secondary group were elderly and already weakened by a chronic debilitating disease.

Despite differences in preoperative conditions affecting surgical risk, the preparations for splenectomy in cases of primary and secondary hypersplenism are similar. Individual considerations must be given, however, to the specific cytopenias, with special preparations for patients with thrombocytopenic purpura and hemolytic anemia.

THROMBOCYTOPENIC PURPURA

In patients with thrombocytopenic purpura there is a marked lowering of blood platelets predisposing to hemorrhage into the skin, mucous membranes, and central nervous system. These patients often present an alarming situation to the surgeon with limited experience in hypersplenism. There was a bleeding tendency in 100% of our 57 patients with evidence of bleeding into the skin or from the mucous membranes (fig. 4). Furthermore, in 46% of these patients the platelet count was 0 to 10,000 per cubic millimeter at the time splenectomy was

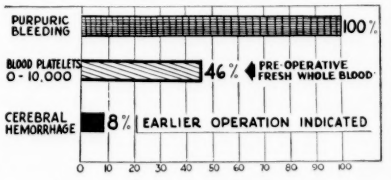

Fig. 4.—Preoperative conditions in 57 patients with thrombocytopenic purpura. The high incidence of bleeding tendency and markedly lowered blood platelets clearly shows the alarming situation encountered by the surgeon. Cerebral hemorrhage, occurring in nearly one out of 10 cases preoperatively, indicates the need for earlier operation.

accomplished. Although fresh whole blood transfusions immediately preceding and during the operation may raise the platelet count to a limited extent, these patients must frequently be accepted for operation despite the absence of platelets. Since cerebral hemorrhage is a

definite threat in the patients with markedly lowered circulating blood platelets, early or emergency splenectomy may be advised by the hematologist. Cerebral hemorrhage occurred in 8% of the 57 cases of thrombocytopenic purpura, clearly indicating the need for earlier operation. Although the patient may show evidence of an extensive cerebral hemorrhage, this is no contraindication to splenectomy, since marked improvement may usually be expected to follow operation and since prevention of further such episodes will be accomplished. Two patients, one with hemiplegia and another in coma, with acute cerebral hemorrhage due to thrombocytopenia, responded to splenectomy with complete return of neurological function. Unnecessary delay of splenectomy for the replacement of platelets by fresh whole blood transfusions may prevent the patient from ever reaching the operating table. The surgeon can proceed with confidence despite the absence of platelets provided the diagnosis, as previously mentioned, has been substantiated by bone marrow and other studies routinely carried out by the hematologists.

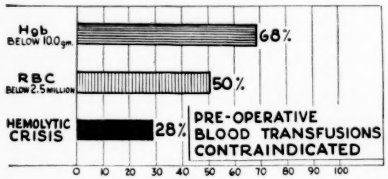

Fig. 5.—Graphic representation of the poor surgical risk in 50 cases of hemolytic anemia owing to the preoperative lowered hemoglobin and red blood cell count, which cannot be brought to higher levels by transfusions because of the danger of precipitation of a hemolytic crisis.

HEMOLYTIC ANEMIA

The hypersplenic patient with hemolytic anemia presents a special problem, which may be even more trying to the surgeon than that presented by a patient with thrombocytopenic purpura. There were 50 cases of hemolytic anemia in this group of 144 patients. Despite the fact that severe anemia frequently exists in these patients, preoperative transfusions are usually contraindicated, because of the danger of precipitation of a hemolytic crisis. As a result, transfusions cannot be given to raise the hemoglobin and red cell count to the normally accepted levels believed safe for major abdominal surgery. As a matter of fact, the hemoglobin level was below the minimal acceptable standard of 10 gm. in 68% of these 50 patients (fig. 5). Furthermore, in 50% of the patients, the red cell count was below 2.5 million. Occasionally it may be necessary for the surgeon to accept a patient with hemolytic anemia for splenectomy despite the fact that the red cell count may be at a level of one million or even lower, especially in the presence of an acute hemolytic crisis.

The precipitation of a hemolytic crisis by the transfusion of matched blood or even resuspended cells presents a greater danger than does the undertaking of splenectomy in the patient with severe anemia. Twenty-eight per cent of these patients already had a hemolytic crisis, even though transfusions had not been given. The danger of further crisis from transfusions is a real one, and there seems no way to determine prior to transfusion in which patients transfused blood will not hemolyze. Several of the patients with secondary acquired hemolytic anemia were given transfusions prior to the confirmation of the diagnosis of hypersplenism or with the hope that slowly given transfusions might raise the hemoglobin level and better prepare the patient for surgery. In three patients, severe hemolytic reactions occurred. In two of these this resulted in severe icterus and a hemoglobin and red cell count lower prior to operation than at the time of admission to the hospital. Experience has shown that splenectomy in these patients without preoperative transfusions is wiser.

The transfusion of whole blood is now avoided until after the ligation of the splenic artery. It is obvious, therefore, that the surgeon must be prepared to perform splenectomy with a minimum of blood loss. Furthermore, he must have a thorough understanding of the anatomy to facilitate the approach to the splenic artery, in order that it may be rapidly ligated and transfusions can be given. As soon as the splenic artery is ligated the hemolytic process is stopped, and the remainder of the operation can be safely continued.

SPLENIC NEUTROPENIA

The use of antibiotics to control the frequent recurrent infections seen in patients with splenic neutropenia and associated with the lowered neutrophil counts is of the greatest importance. Transfusions may be given to patients with splenic neutropenia, in contrast to hemolytic anemia and thrombocytopenic purpura, at any time they are needed, but it should be realized that no significant rise in the white cell count will be effected by transfusions.

The neutrophil count in these patients may vary considerably from time to time, with frequent remissions of the neutropenia. For this reason, splenectomy is usually safer when performed while the neutrophil and total leukocyte counts are at one of their higher peaks; at this time postoperative infections are less likely to occur. However, operation should not be delayed in those cases in which severe neutropenia persists.

Of the 27 cases of splenic neutropenia, 20 were associated with other chronic disease processes, thus showing the greater incidence of secondary splenic neutropenia as compared with primary neutropenia. There were 10 cases in which Banti's disease was associated with secondary neutropenia. The development of a routine technique of splenectomy for all types of hypersplenism, with painstaking technique, including delayed ligation of the splenic vein, has made possible the utilization of this vein in the performance of a venous shunt in the presence of portal hypertension. A splenorenal venous anastomosis has been performed in six patients with Banti's disease. Only two of these patients had hypersplenism associated with the Banti's disease, and these two patients are described in this report.

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PANHEMATOCYTOPENIA

Panhematocytopenia, presenting a depression of all the circulating formed elements, is the least common of the forms of hypersplenism. In the four cases of primary panhematocytopenia and four cases of secondary panhematocytopenia, the indications for transfusions and antibiotics in the preoperative period were carefully determined by the hematologists. Although it should be realized that, if thrombocytopenia predominates, fresh whole blood is desirable, and, if anemia predominates, transfusions may best be deferred; these decisions must rest in the hands of a competent hematologist.

PREOPERATIVE NASAL GASTRIC INTUBATION

The use of a nasogastric tube to decompress the stomach prior to and during the operation is dependent on the individual type of cytopenia and other complicating pathological processes. Such intubation facilitates operative exposure by decompression of the stomach and also decreases the possibility of hemorrhage from the short gastric arteries. In order to avoid incurring hemorrhage in patients manifesting either thrombocytopenic purpura or esophageal varices, we do not usually employ intubation. However, if after the abdomen is opened the stomach is found to be markedly distended, we have not hesitated to have the anesthetist introduce a gastric tube for deflation, in order to facilitate the safe and rapid approach to the region of the splenic artery. The problem of gastric distention appears to be more frequently encountered in children.

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ANESTHESIA

Anesthesia for splenectomy often is associated with considerable technical difficulty, because of the frequent occurrence of severe anemia or debility in these patients. It is of utmost importance to maintain a good airway and an adequate oxygen intake.

In patients with a severe bleeding tendency, there may be bleeding from the nose, gums, and pharynx before the induction of anesthesia. The presence of clotted blood and bloody mucus must not be allowed to produce mechanical obstruction of the respiration. The patient should not be allowed to aspirate this material into his tracheobronchial tree. Suction cleansing of the nose, mouth, and pharynx should be very gently carried out to remove the fluid material. Clotted blood around the gums should not be disturbed, because fresh bleeding may be started. The patient must be handled very gently, and excitement stage should not be allowed to take place. Nasal pharyngeal and oral pharyngeal airways and endotracheal tubes should not be inserted, because their presence may induce bleeding. In cases in which an adequate airway cannot be maintained, an endotracheal tube should be very gently inserted.

The most satisfactory anesthetic procedure for splenectomy has been the induction of anesthesia with thiopental sodium followed by the use of cyclopropane for maintenance. Curare or one of its derivatives is used to provide relaxation, and ether may be added to the anesthetic mixture if necessary. Endotracheal intubation is performed in those patients who do not have a bleeding tendency, in order to insure a clear airway and to permit supplemented respiration. The quantity of anesthetic required by many of these anemic and debilitated patients is less than usual. A light plane of anesthesia is maintained with cyclopropane, and doses of curare are administered that are adequate to provide good relaxation. It is of utmost importance that a high oxygen content in the gas mixture be maintained and that adequate respiratory exchange should take place.

SPECIAL CONSIDERATIONS OF OPERATIVE TECHNIQUE

The patient is placed on the operating table with a pillow under the knees and is kept in a moderate degree of reverse Trendelenberg position over an elevated gallbladder rest. A left paramedian incision is made, extending from high in the xiphocostal angle to the umbilicus. In no instance has it been necessary to use a combined thoracoabdominal incision. Hemostasis in the wound must be rigidly observed, but necesssary prolongation of the operation by application of clamps to every minute bleeding point is unnecessary. Less blood loss may occur with careful compression of gauze packs applied to the wound edges. This is especially important in the patients with thrombocytopenic purpura. No serious bleeding occurred in our 57 cases of thrombocytopenic purpura. Since there is usually a prompt improvement in the patient's hematological status after ligation of the splenic artery and removal of the spleen, the ligation of the major vessels in the wound to which clamps have been applied may be deferred until the time of closure.

Since the hematological picture rapidly and frequently dramatically improves after ligation of the splenic artery, the surgeon should proceed directly to accomplish this, with delay of a general abdominal exploration until after the splenectomy. It has been our practice to grasp the stomach with Babcock forceps opposite the spleen, in order to define more clearly the gastrosplenic ligament. Clamps are applied to the short gastric vessels as close to the stomach as possible, in order that those on the gastric side may be ligated by transfixation of sutures which include bites of the gastric wall. This technical step is important, since insecure ligatures may slip should postoperative gastric distention occur. As soon as a window of sufficient size has been made into the lesser sac, retractors are inserted to pull the stomach upward and the colon and pancreas downward, to permit visualization of the superior margin of the pancreas. While the splenic artery is often large and tortuous, especially in the older age groups, it may be necessary to determine its location by palpation in the very obese patient. The most readily accessible point is selected for ligation, regardless of the distance from the hilus of the spleen. The peritoneum is incised, and, with the use of a right angle clamp as a blunt dissector, a segment of the splenic artery is dissected free, in order that a silk suture may be pulled through and subsequently tied.

The ligation of the splenic artery as one of the initial steps in splenectomy offers many advantages. In the first place, whole blood transfusions may be started in patients with low blood levels, especially those with hemo-

lytic anemia. Second, the hematological picture almost immediately begins to improve and oozing due to low platelet levels usually stops. Third, there is probably less blood loss with subsequent steps of the operation, as a result of decreased pressure within the spleen itself. Fourth, splenic contraction ensues and provides an efficient method of providing an autotransfusion to the patient. Finally, ligation of the splenic artery results in firm contraction of the spleen with better definition of the various splenic ligaments, thus lessening the chance of rupture of the splenic capsule during its removal.

The surgeon should routinely utilize a technique of splenectomy applicable to the establishment of a venous shunt, using the splenic vein when indicated. Although rapid mobilization and mass ligation of the splenic pedicle may be advisable in the presence of a ruptured spleen, the routine use of a painstaking technique with individual ligation of vessels will pay rich dividends, regardless of the indications for splenectomy. This is important for a number of reasons: (1) to keep blood loss to a minimum, (2) to assure a clean field free of hematomas, in order that accessory spleens may be more easily identified, (3) to avoid possible injury to the tail of the pancreas or the greater curvature of the stomach, where it is intimately attached to the upper pole of the spleen, and (4) to delay ligation and conserve as much as is required of the splenic vein for a splenorenal venous shunt, which will be needed in cases of hypersplenism associated with Banti's disease.

After ligation of the splenic artery, the uppermost portion of the gastrosplenic ligament is divided and the contents of each pair of clamps ligated, in order to permit clear visualization of the entire field free of clamps at all times. After this, the spleen is retracted toward the midline and the splenorenal ligament divided. Unless there are dense adhesions or portal hypertension, it is usually unnecessary to ligate any vessels in this ligamentous attachment. Great care must be exercised during this manipulation of freeing the spleen, lest the splenic capsule be torn and excessive loss of blood occur or remnants of splenic tissue be left behind. Such remnants may persist, resulting in splenosis and the danger of possible recurrence of the hypersplenism. After the spleen has been well mobilized into the wound, the tail of the pancreas should be separated gently from its splenic attachment and any small pancreatic veins ligated. In some cases of leukemia the hilus of the spleen may be filled with lymph nodes, which tend to obscure the usual anatomic landmarks. The spleen is compressed by an assistant as firmly as possible, in order to provide the patient with the greatest amount of blood as an autotransfusion until the splenic vein is doubly ligated. The splenic vein is the last vessel in the pedicle that is divided. The contents of all clamps are double ligated with a simple tie of no. 3-0 silk proximally and a transfixing suture distally.

During the splenectomy, one or more accessory spleens are commonly encountered and often removed with the spleen. However, regardless of whether an accessory spleen has been previously noted, a careful search must be made for any persisting accessory spleen. If an accessory spleen is left in the patient, the same disease process may recur several weeks to several years later.

The locations of accessory spleens and their identifications are important to the surgeon who performs splenectomy. Accessory spleens will be found in the following places, in the order of frequency: the splenocolic ligament, the retroperitoneal space at the under surface of the tail of the pancreas, the gastrocolic ligament, the gastrosplenic ligament, the hilus of the spleen, the splenorenal ligament, the greater omentum, and overlying the left kidney. The experienced surgeon should be able to differentiate between lymph nodes, hemolymph nodes, and accessory spleens. All may be multiple in number, and, when there is any question as to the identity, they should be removed. As many as 31.4% accessory spleens have been found and reported by Curtis and Movitz.[5] They were found in 20% of our patients with hypersplenism and were more frequent (23%) in patients with primary hypersplenism.

At this time the entire abdomen is explored and the gallbladder palpated for the presence of stones. This is especially important in the patient with hemolytic icterus. Stones are frequently found and have been reported to occur in cases of hemolytic icterus with a frequency of 71%.[6] In our patients, only 18.5% were found to have gallstones. When the general condition of the patient was good, and exposure easy, we have on occasion removed the gallbladder at the time of splenectomy, but ordinarily this has been deferred.

Other essentials necessary before closure of the abdomen consist of biopsies of the liver, retroperitoneal lymph nodes, and a mesenteric lymph node. Studies of these biopsy specimens by the hematologist are of great value in the determination of the status of the reticuloendothelial system and on occasion, by the discovery of a lymphosarcoma, Hodgkin's disease, or some other primary disease, may convert the diagnosis of primary hypersplenism to one of secondary hypersplenism. In addition, should the hematological picture not improve in a satisfactory manner, a study of these biopsy specimens may enable the hematologist to make a better prognosis. This follows, since overactivity of the reticuloendothelial system in general implies that removal of the spleen cannot be counted on for certain to improve the hematological state for which the splenectomy was performed. Of special importance is the biopsy of the retroperitoneal lymph nodes. Ordinarily these are more easily found and are more readily accessible along the upper margin of the pancreas. In the majority of instances an opening is made through an avascular portion of the hepatogastric ligament, the stomach is retracted down, and the peritoneum is divided over the lymph nodes invariably present above the pancreas. A liberal portion of the nodes is removed as a specimen. It has been our experience that the diagnosis of lymphosarcoma or Hodgkin's disease is more likely to be made from the retroperitoneal nodes than from those removed from the mesentery of the upper jejunum.

5. Curtis, G. M., and Movitz, D.: The Surgical Significance of the Accessory Spleen, Ann. Surg. **123**: 276 (Feb.) 1946.

6. Pemberton, J. de J., and Kiernan, P.: Surgery of the Spleen, S. Clin. North America **25**: 880 (Aug.) 1945.

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Abdominal drainage is not used, and retention sutures are used only in debilitated patients with secondary hypersplenism. Three zero and four zero silk suture material is utilized throughout.

RESULTS

Satisfactory postoperative hematological results were obtained in 91% of the patients with primary hypersplenism and 64% of the patients with secondary hypersplenism. In the subgroup, acquired hemolytic icterus, only three out of seven (42%) showed good results. These figures show only an early trend, and late results lie in the field of hematology.

The surgical morbidity and mortality of splenectomy differ significantly in cases of primary and secondary hypersplenism (see accompanying table). As might be expected, the results in patients with secondary hypersplenism, though satisfactory, are not as good as those in patients with primary hypersplenism.

Postoperative recovery in most of the patients was rapid and ambulation early, except in those with long-standing leukemia or Hodgkin's disease. The average hospital stay was 10 days for those with primary and 14 days for those with secondary hypersplenism.

Postoperative complications occurred in 6.6% of patients with primary hypersplenism and 21% of those with secondary hypersplenism. Results can be closely correlated with the preoperative conditions; yet many patients who might be considered extremely poor surgical risks have undergone splenectomy with gratifying outcomes. Many of the patients with chronic leukemia, Hodgkin's disease, Banti's disease, and Boeck's sarcoid were in an advanced stage of the primary disease at the time of splenectomy. A few of the leukemic patients were almost moribund at the time of splenectomy from the combination of leukemia and associated hypersplenism, and marked improvement of the patient's general condition followed splenectomy. One patient previously reported,[7] a 24-year-old white woman with primary thrombocytopenic purpura, was seven months pregnant at the time of surgery. She had manifestations of cerebral hemorrhages with feared placenta previa, and surgery had to be done as an emergency. She recovered without incident, and her pregnancy went to term satisfactorily without recurrence of bleeding.

Results in Fifty-Four Cases of Secondary Hypersplenism and Ninety Cases of Primary Hypersplenism

	Secondary Hypersplenism	Primary Hypersplenism
Average postoperative hospital stay.....	14.0 days	10.0 days
Postoperative complications	21%	6.6%
Postoperative deaths	13%	1.1%

The most frequent complications were pneumonia, atelectasis, abdominal distention, pulmonary embolism, and myocardial infarction. Postoperative hemorrhage occurred in only two cases, in one from the upper gastrointestinal tract and in one from the tail of the pancreas. Hematoma formation in the operative site did not occur in any of the patients with thrombocytopenic purpura.

The postoperative mortality likewise has been sharply different in patients with primary and secondary hypersplenism. With primary hypersplenism, the mortality was only 1.1%, and with secondary hypersplenism the mortality was 13%. The only death in the former occurred after splenectomy in a 70-year-old white woman with pneumonia and extensive cerebral hemorrhage prior to operation; in this case surgery was performed for idiopathic thrombocytopenic purpura. In secondary hypersplenism there were seven deaths in 54 patients. One death was due to pulmonary embolus, one to myocardial infarction, one to so-called liver failure, one to gastrointestinal hemorrhage, one to anesthesia, and two to postoperative pneumonia. The seven patients comprised four with Banti's disease and three with advanced chronic lymphatic leukemia.

SUMMARY

Experience on the general surgical service of the University Hospital with 144 consecutive patients with hypersplenism over a four and one-half year period is reported. Splenectomy was performed in every case. Particular emphasis has been placed on the necessity of close teamwork between hematologist and surgeon for best possible results. Those diseases included under both primary and secondary hypersplenism are discussed from the viewpoints of incidence, age groups, special problems in preoperative care, and results.

A method of splenectomy stressing painstaking technique, with early ligation of the splenic artery and individual ligation of the vessels in the splenic pedicle, a careful search for accessory spleens, and routine liver and lymph node biopsies is outlined. The over-all postoperative mortality in this series was 5.5%; the mortality in the 90 patients with primary hypersplenism was 1.1%; and that in the 54 patients with secondary hypersplenism was 13%. It has been our experience that excellent results may be realized with splenectomy in cases of primary hypersplenism; satisfactory though admittedly poorer results may be expected in the more difficult group of cases of secondary hypersplenism.

7. Barnes, A. C.; Wiseman, B. K., and Zollinger, R. M.: Splenectomy in Pregnancy: A Case Report, Health Center J. 3: 94 (June) 1950.

Right Rectus Rigidity.—Increased tonus of the abdominal muscles, or so-called rectus rigidity, is not a sign of acute appendicitis, but rather a sign of peritonitis. We know that it is quite impossible to contract one rectus muscle without contracting the other. Why then do we refer to the sign as right rectus rigidity when both recti contract? To correctly test for this sign the examiner must place both of his hands on the abdomen, one on each rectus muscle. With gentle pressure he determines whether or not one rectus is rigid and the other relaxed. If such a condition exists and only one rectus muscle is found to be rigid, then this suggests a mass underlying the rigid rectus. Such masses in the case of acute appendicitis would be either a localizing inflammatory appendical mass made up of appendix, terminal ileum and omentum, or an appendical abscess. When both recti are rigid it denotes a muscular defense in response to an underlying peritonitis. Should such a rectus suddenly be released the patient will wince because of so-called rebound tenderness (Blumberg's sign).—Philip Thorek, M.D., Acute Appendicitis, *The Illinois Medical Journal*, November, 1951.

INFANTILE CEREBRAL PALSY

CLASSIFICATION AND CLINICAL CORRELATIONS

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Cerebral palsy may be defined as a condition characterized by paralysis, paresis, incoordination, dyskinesia, or any aberration of motor function that is due to involvement of the motor control centers of the brain. It should be differentiated from spinal palsies, such as poliomyelitis or transection of the cord, and from peripheral nerve palsies, such as peripheral neuritis due to lead poisoning or diphtheria. Since the brain has many functions in addition to control of motor ability, it is not surprising that in the cerebral palsied there may be many associated defects. Defects in intelligence, personality, and sensation or epileptic diatheses may coexist. In addition, there may be many sequelae of cerebral palsy, such as physical deformities due to contractures and personality defects incident to the lack of opportunity for normal social development. The present paper, however, is limited to a consideration of the classification and specific etiological correlations of the motor symptoms of cerebral palsy as they occur in the infantile forms of the condition.

Much confusion exists in the terminology and classification of the various forms of cerebral palsy. The term "Little's disease" [1] has often been used as a generic term to include all forms of cerebral palsy. Actually, what Little described was only one of the many types of the malady. The term "spastic" is often used by the doctor and layman to cover all categories of cerebral palsy. This tendency is conducive to loose thinking. A logical classification of the types of cerebral palsy would help clarify this confused subject.

Cerebral palsy may be classified according to various criteria, depending on the emphasis and viewpoint desired. It may be classified according to ((1)) the anatomic site of the brain lesion; ((2)) the qualitative nature of the clinical symptom present, whether spasticity, athetosis, rigidity, etc.; ((3)) the topographical involvement of the extremities; ((4)) the degree of tonicity; ((5)) the severity of involvement; and ((6)) the etiology. Each of these classifications has certain advantages and certain disadvantages, and it is in the overlap of the various classifications that many of the clinical correlations in the field of cerebral palsy may be observed.

I. CLASSIFICATION ACCORDING TO ANATOMIC SITE OF BRAIN LESIONS

Cerebral palsy may be classified according to the portion of brain that is involved and thus, presumably, responsible for the symptoms. According to this classification, cerebral palsy may be divided into three general categories:

A. Pyramidal Tract Involvement.—Clinically, patients with pyramidal tract involvement, either in cortical regions in the precentral gyrus or subcortically in the region of the internal capsule, are the true spastics (see Clinical Classification below), and the clinical syndromes are presumably due to removal of the inhibitory effects of the pyramidal tract.

B. Extrapyramidal Tract Involvement.—This covers involvement primarily, of the basilar nuclear areas and/or their connections. Clinically this classification covers patients with abnormalities of motion, such as athetosis, choreas, tremors, ballismus, dystonias, and rigidities. Presumably, the exact clinical picture depends on the specific area involved, e. g., lesions of the corpora striata may cause certain types of tremors, and lesions of the globus pallidus may cause rigidity.

C. Involvement of the Cerebellum and/or Its Connections.—Clinically this classification would include primarily ataxias and the atonic forms of cerebral palsy.

Comment.—The disadvantage of this classification is that it presumes a knowledge that we really do not have. It is based on the previous orthodox concepts of localization of function of the brain, many of which have recently been changed. Patients have been seen with the clinical diagnosis of "extrapyramidal rigidity" and the pathological finding of aplasia of the cerebellum. Other patients with athetoid and choreiform motions were found on postmortem examination to have normal basal nuclei and only cortical lesions. Thus, until further knowledge of the functions of various portions of the brain is acquired, a classification based on morbid brain anatomy can be only of didactic value.

II. CLASSIFICATION ACCORDING TO CLINICAL SYMPTOMS

This classification is based on the observable outstanding clinical symptoms and may be subdivided into (1) spastic conditions, (2) dyskinesias, and (3) ataxia.

A. Spastic Conditions.—These are characterized by the clinical signs attributed to "upper motor neurone" involvement. Specifically, there is present a stretch reflex in the involved muscle.[2] This stretch reflex is characterized by an increased tendency of the muscle to contract when it is passively stretched rapidly. This reflex is not present when the muscle is passively stretched slowly. The stretch reflex is not limited to the stretched muscle alone, but tends to spread to contiguous muscles, with the result that a mass motion of the whole extremity may occur. Electromyographically the stretch reflex can be recognized as a marked increase in the amplitude and spread of the normal action current of the muscle. The stretch reflex is more commonly found in the antigravity muscles, such as the quadriceps and gastrocsoleus group, than in their antagonists. In addition, ankle clonus, in-

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creased deep reflexes, and the Babinski sign may be present. Superficial reflexes may be present or absent. In the spastic form of cerebral palsy, muscle contractures are commoner than in other forms. Convulsive episodes and mental retardation are also commoner in the spastic form, particularly in patients with marked hand involvement.[3]

B. Dyskinesias.—In this group the characteristic clinical finding is an abnormal amount and type of motion. The muscle per se reacts in perfectly normal manner so far as reflexes and muscle contraction are concerned. Electromyographically there are no abnormalities. There is marked abnormality, however, in spontaneous motion, which may be totally increased, totally decreased, or simply aberrant in nature. The two main factors that are responsible for these abnormalities of motion are (1) the tendency for motions to be uncontrollable, involuntary, and incoordinate and (2) the tendency for various degrees of tension or rigidity to occur during the performance of these motions. As a result, bizarre patterns of motion may appear, some of them rapid and jerky, some slow and worm-like, and some extremely slow and hypertonic. The motions may be unpredictable, or they may be rhythmic in character and of various amplitudes. Although many names have been given to describe some of these characteristics, there is no clear-cut line between these various forms, which merge imperceptibly into each other and which may vary in a given patient from day to day.

1. Choreas: These are characterized by involuntary, uncontrollable, sudden, jerky, unpredictable, purposeless, and random movements, rather rapid in nature. In this form it is the hyperkinesia rather than the hypertonicity that predominates.

2. Athetosis: This type of motion differs from that of chorea in that it is associated with more tension. As a result, the motions are slower and more writhing or worm-like than those of chorea, but like those of chorea are involuntary, uncontrollable, unpredictable, and generally purposeless. When the characteristic of the motion is that of a large amplitude or flailing motion, the term ballismus is often employed.

3. Dystonia: In this type of motion, the outstanding symptom is the tension. The muscles are markedly hypertonic, with the result that the involuntary motions are very slow, to the point that the patient may assume tonic postural attitudes. In this type the axial musculature is more involved than that of the limbs.

4. Tremors: These are uncontrollable, involuntary motions of a rhythmic alternating or pendular pattern. They are due to alternate agonist and antagonist contractions.

In the above forms of dyskinesia the involuntary motions and the hypertonicity are diminished when the patient is asleep or at rest and are increased on attempts at voluntary motion. In these patients voluntary attempts to move a single extremity may be associated with an initiation or aggravation of involuntary motions in the other extremities (athetoid shift). However, the reciprocal agonist and antagonist relationship between the muscles is maintained, so that relaxation in the antagonist accompanies contraction of an agonist muscle.

5. Rigidity: Extrapyramidal rigidity is characterized by disturbance in the agonist-antagonist relationships. There is resistance to slow passive motion of both agonist and antagonist muscles. This resistance is greater to slow than it is to rapid passive motion, a clinical finding that is diametrically opposed to that found in the spastic muscle, where the greater resistance is to rapid motion. Rigidity differs from spasticity also in that the antagonists to the antigravity muscles are involved most. The outstanding clinical finding in rigidity is the hypertonicity of the muscle rather than the excessive motion. In fact, in rigidity, total motion may be decreased.

At times, the resistance to passive motion in extrapyramidal rigidity is continuous, simulating the sensation of bending a lead pipe. This is referred to as the "lead pipe" type of rigidity. At other times there may be a discontinuous type of resistance, simulating a cogwheel type of action, and therefore designated as "cogwheel" rigidity. As with most forms of dyskinesia, the degree of rigidity may vary from time to time, being marked at one instant and not discernible at the next instant. The term "intermittent rigidity" denotes this characteristic.

C. Ataxia.—The outstanding symptom in patients with this condition is a disturbance in sense of balance and equilibrium. Dyssynergias, past-pointing, and intention tremors are frequently present. The patient often exhibits the "rebound phenomenon," with inability of the antagonist to stabilize a joint after sudden release of resistance to an agonist. Stereognosis and depth perception may be involved. In addition, there may be loss of muscle tone, so that atonia or hypotonia may be present. Although ataxia is due presumably to involvement of the cerebellum and/or its tracts, it is possible for certain higher brain lesions to be associated with forms of ataxia. Likewise, some of the conditions that are clinically rigidity, or even spasticity, may be due to cerebellar lesions, involving motor excitatory and suppressor regions in the cerebellum.[4]

Spasticity and ataxia usually appear as pure clinical syndromes, but the various forms of dyskinesia may occur together in the same patient, one form predominating one day and another the next. Although there may be mixed cases in which spasticity, athetosis, and ataxia may coexist, such is the exception rather than the rule. This may be due in part to the predilection of certain etiological factors to cause specific lesions, and in part to the fact that a lesion, to cause mixed clinical symptoms, might be so extensive as to be fatal.

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2. Magoun, H. W., and Rhines, R.: Spasticity: The Stretch-Reflex and Extrapyramidal Systems, American Lecture Series No. 9, American Lectures in Physiology, Springfield, Ill., Charles C Thomas, Publisher, 1948.

3. Perlstein, M. A.; Gibbs, E. L., and Gibbs, F. A.: The Electroencephalogram in Infantile Cerebral Palsy, Proc. A. Res. Nerv. & Ment. Dis. **26**: 377, 1946.

4. Snider, R. S.: Recent Contributions to the Anatomy and Physiology of the Cerebellum, Arch. Neurol. & Psychiat. **64**: 196-219 (August) 1950; Recent Contributions to Our Knowledge of the Cerebellum, Monthly Research Report of the Office of Naval Research, Department of the Navy, p. 15 (Aug. 1) 1950.

III. CLASSIFICATION ACCORDING TO TOPOGRAPHICAL INVOLVEMENT OF EXTREMITIES

At times the qualitative nature of cerebral palsy may be indicated by the topographical distribution of the involvement. In some instances, legs are more involved than arms, and in others, one side more than the other. Various terms have been used to describe these clinical pictures. These terms are more or less empirical and are defined in accordance with general usage.

A. Paraplegia.—This involves the legs only. Cases of paraplegia are practically always of the spastic variety.

B. Diplegia.—This involves the legs primarily and the arms to a slight extent. Cases of this type are generally of the spastic variety.

C. Quadriplegia, or Tetraplegia.—This involves all four extremities. Patients with greatest involvement of the legs are usually spastics, and those with greatest involvement of the arms usually have dyskinesias. (Thus, paraplegia, diplegia, and quadriplegia, with more involvement of the legs, may be considered ascending grades of the same condition.)

D. Hemiplegia.—This condition is lateralized to one-half of the body. Hemiplegics have greater involvement of the arm and are usually spastic. Occasionally there may be an associated dyskinesia on the involved side; when this occurs, it affects primarily the arm. Pure athetoid hemiplegias are occasionally seen. In hemiplegias that are acquired congenitally or early in life, there is usually a decreased rate of growth of the involved side of the body, the arm being more affected than the leg. The discrepancy in the length of the two arms may be one of the most reliable and constant signs in the diagnosis of mild infantile hemiplegia. This "atrophy" cannot be explained on the basis of disuse, since it is often disproportionate to the amount of disuse. More likely, involvement of a "developmental center" in the postcentral gyrus of the contralateral portion of the brain is responsible.[5]

Sensory involvement on the affected side is not uncommon in hemiplegia, particularly in the areas of proprioception, two-point discrimination, and form perception. Aphasias occur more frequently in right than in left hemiplegia and more frequently in acquired than in congenital hemiplegia.

E. Triplegia.—This involves three extremities. Usually both legs and one arm are involved, and these are generally spastic. Triplegia may in reality represent a combination of a hemiplegia plus paraplegia, or it may represent incomplete quadriplegia, sparing one arm. In the latter event, both arms will be of equal or nearly equal length, whereas, in the former, the arm that is involved will be appreciably shorter than the uninvolved side. Although these considerations may appear to be of only didactic importance, they have etiological significance.

5. Penfield, W., and Erickson, T. C.: Epilepsy and Cerebral Localization: A Study of the Mechanism, Treatment, and Prevention of Epileptic Seizures, Springfield, Ill., Charles C Thomas, Publisher, 1941, pp. 49-50.

F. Monoplegia.—This involves one limb and is extremely rare. When it does occur, it usually involves one leg and spasticity. In most cases in which the condition is thought to be monoplegia, closer inspection will reveal it to be either mild paraplegia or hemiplegia.

G. Double Hemiplegia.—This term is reserved for cases of spastic quadriplegia, in which the arms are more involved than the legs. This is contrary to the rule that most cases of quadriplegia with greater involvement of the arms are athetoid cases, and those with greater involvement of the legs are spastic. Thus, a spastic quadriplegic with greater involvement of the arms may be considered as having hemiplegia on both sides, since in the spastic hemiplegic the arm is more involved than the leg.

H. Infantile Cerebral Palsy Limited to Both Upper Extremities.—Since this is practically never encountered, a name for this category is superfluous.

Comment.—There is a close correlation between the incidence of convulsions, educability and the topographic involvement of cerebral palsy. In general, the incidence of convulsions is higher and intellectual involvement greater where hand involvement is greater. Thus, in paraplegics, there are fewer convulsions and less mental deficiency than in hemiplegics or in quadriplegics. However, in athetoids as a class, the incidence of convulsions and mental deficiency is lower than in spastics.

IV. CLASSIFICATION ACCORDING TO DEGREE OF MUSCLE TONE

One of the characteristic findings in cerebral palsy is a change in muscle tone. The state of muscle tone may be classified as (*a*) isotonic, or normal tone; (*b*) hypertonic, or increased tone, often referred to as "tension" type; and (*c*) hypotonic, or decreased tone; when it is pronounced, it is often referred to as "atonic."

The appearance of hypertonicity or hypotonicity may precede the appearance of dyskinesia or spasticity. Thus, in infants under one year of age, athetoid motions may be difficult to detect, but increased muscle tension on attempts at voluntary motion may be easy to elicit. Abnormalities in tone of a muscle may modify extraneous or incoordinate motions into distorted patterns.

When tone increase is maximal, the dystonic forms of cerebral palsy may be present. In the presence of hypotonia, extraneous motions may be so decreased that athetosis becomes evident only when the muscle becomes tense, as on attempted voluntary motion. In atonic spastic diplegia, the hypotonia may be so marked that the condition simulates amyotonia congenita. The differential diagnosis between these two latter conditions is based on the presence of the stretch reflex and increased deep reflexes in atonic spastic diplegia and their absence in amyotonia congenita. Moreover, the patient with amyotonia congenita does not have the ability to develop increased or even normal muscle tone on attempts at voluntary movement, as may the cerebral palsied patient with hypotonia. Abnormalities in muscle tone are apparently independent of the state of spasticity or dyskinesia.

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V. CLASSIFICATION ACCORDING TO SEVERITY OF INVOLVEMENT

This classification is entirely empirical and means more to the person who describes the patient than to the person who reads the description. In general, however, one can divide degree of involvement into three grades, with numerous intermediate steps.

A. Mild.—The patient is able to ambulate, to use his arms, and to speak well enough to need no special care.

B. Moderate.—Involvement is severe enough to handicap the patient in locomotion, self-help, or communication, but not sufficient to disable him entirely. Such patients will need some special care.

C. Severe.—There is total involvement, and the patient is incapacitated, being bedridden or restricted to a wheelchair. Complete habilitation, by any means of treatment, may not be possible in such patients.

VI. CLASSIFICATION ACCORDING TO ETIOLOGY

This is one of the most useful classifications of cerebral palsy, since specific etiological factors often cause characteristic clinical syndromes. From a temporal viewpoint, the etiological factors can be divided into those that operate prenatally, natally, or postnatally.

A. Prenatal.—Prenatal factors are those operating from the time of conception to the time of labor. These are responsible for approximately 30% of all cases of cerebral palsy and may be due to genetic defects or to injuries acquired in utero.

1. Hereditary: By hereditary conditions are meant those that are genetically transmitted, may involve racial or familial predilections, and are often sex-linked. These may be either static or progressive in nature. The clinical syndromes seen usually have specific morbid entities that can be recognized pathologically. The term "cerebral agenesis" may be applied to these conditions.

(*a*) Static. In this type the symptoms are present at birth or soon after, and do not progress, e. g., hereditary athetosis, familial tremors, and familial spastic paraplegia.

(*b*) Progressive. Symptoms may or may not be manifest at birth but may appear in later life. They are progressive and generally fatal, e. g., Tay-Sachs disease, demyelinating diseases, and tuberous sclerosis.

2. Acquired in Utero: (*a*) Prenatal infection. Examples are toxoplasmosis, rubella, or other maternal infection. Most of the maternal infections that involve the child are those that are experienced by the mother in the first trimester of pregnancy.

(*b*) Prenatal anoxia. Any factor that interferes with proper oxygenization of the mother will obviously be a cause of anoxia in the fetus. Thus, carbon monoxide poisoning or strangulation of the mother, or maternal anemia, or hypotension as might follow spinal anesthesia are all potential causes of fetal anoxia. In addition, placental pathological conditions, such as infarcts or placenta abruptio, as well as kinking of the cord, may all result in damage to the fetal brain.

(*c*) Prenatal cerebral hemorrhage. The commonest cause of prenatal cerebral hemorrhage is maternal toxemia of pregnancy. In addition, direct trauma or maternal bleeding diathesis may occasionally be responsible for hemorrhage in the fetal brain.

(*d*) Rh factor or other forms of iso-immunization. Kernicterus due to the Rh factor used to be responsible for about 10% of all cerebral palsy. With improvement in public education and technics of transfusions, it is now responsible for less than 3% of the cerebral palsies. This factor is included in the prenatal causes inasmuch as the maternal antibodies are elaborated in the prenatal period.

(*e*) Metabolic disturbance. An example is maternal diabetes. The manner in which metabolic disturbances of the mother affect the child is not well understood. However, it is known that, when the mother has diabetes, the newborn may occasionally have brain damage. Whether this is related to the greater size of children born to diabetic mothers or to the predilection to toxemia of pregnancy, or to some underlying disturbance in steroid metabolism is not known.

(*f*) Gonadal irradiation. A mother who has been exposed to x-ray therapy may have mutations occurring in the developing ovum that may result in abnormalities in fetal brain development. Although strictly speaking this is genetic, it is still not hereditary and thus is included among the acquired types.

B. Natal Factors.—Natal factors are those that operate from the time of onset of labor to the time of viability of the delivered child. These are the most frequent causes of cerebral palsy and account for approximately 60% of all cases.

1. Anoxia: This is one of the most important causes of cerebral palsy and may be due to many factors: (*a*) mechanical respiratory obstruction due to aspiration of mucus or vernix pneumonias, (*b*) atelectasis, (*c*) narcotism, e. g., after "twilight sleep" or heavy barbiturate dosage, (*d*) placenta previa or abruptio, (*e*) maternal anoxia or hypotension, e. g., following spinal anesthesia, or (*f*) breech deliveries, with delay of the aftercoming head. The mechanism of brain damage in breech delivery is less likely to be mechanical injury than anoxia, since the time from the delivery of the navel to the delivery of the head is a time of potential anoxia.

2. Cerebral Hemorrhage and Contusions: These are perhaps the commonest causes of injury to the brain during the time of delivery.

(*a*) Traumatic. Trauma to the head is inherent in being born and in most instances is due to natural causes. The physiological or natural causes are those that are associated with dystocia, disproportions, malpositioning, and other causes of difficult delivery. In addition, however, obstetric intervention may be responsible for some cases of cerebral palsy. Actually, not over 3% to 5% of all cerebral palsy cases are due to such obstetric factors as injudicious forceps application, "holding back of the head," and induction of labor with posterior pituitary extract.

(*b*) Sudden pressure changes. Precipitate or Cesarean delivery may result in multiple diffuse petechial hemorrhages.

(*c*) Constitutional factors, especially prematurity, may also predispose to cerebral hemorrhage in the newborn.

(*d*) Bleeding tendency in the newborn due to hypoprothrombinemia (vitamin K deficiency) or due to anemias of the newborn may be responsible for damage to the brain.

C. Postnatal Factors.—There are factors operating from the time of the birth of a viable infant. They account for a little less than 10% of all cases of infantile cerebral palsy.

1. Trauma, even though minimal, may often result in subdural hematomas or other brain injury. Skull fractures and penetrating wounds and contusions of the brain following accidents may result in cerebral palsy.

2. Infections of the central nervous system are much commoner in infancy than at any other time of life. Meningitis, encephalitis, and brain abscesses may frequently leave residual damage to the brain.

Common Clinical Correlates in Cerebral Palsy

History	Common Neurological Sequela
Prematurity	Spastic paraplegia
Breech delivery	Athetoid or spastic paraplegia
Toxemia of pregnancy	Spastic hemiplegia
Birth trauma	Spastic quadriplegia or hemiplegia
Anoxia	Athetoid or rigidity
Rh factor	Athetoid with deafness and paralysis of supraversion
Maternal rubella	Spastic with auditory aphasia or deafness, cataract, congenital heart
Precipitate or cesarean delivery	Spastic quadriplegia or rigidity

3. Toxic causes may include chemical poisoning, e. g., lead, arsenic, or coal tar derivatives.

4. Vascular accidents are less common in children than they are in adults. Hemorrhages, when they occur, may be secondary to trauma or, if spontaneous, are generally due to rupture of a congenital aneurysm of the circle of Willis. Vascular spasm may occur in hypertensive encephalopathies. Emboli, when they occur, are more likely to be due to bacterial endocarditis or to fat embolism following trauma. Thrombosis of cerebral vessels is most commonly seen in debilitated, marantic, or syphilitic infants. Sudden pressure changes, such as those associated with blast injuries, may also be responsible.

5. Anoxia occurring in postnatal life has similar effects to those occurring prenatally or natally. Thus, carbon monoxide poisoning, strangulation, or high altitude and deep pressure anoxias will have similar effects on the brain. Children who have spontaneous or insulin hypoglycemia may also show signs of permanent brain injury, the mechanism that results in damage probably being similar to that of anoxia.

6. Neoplastic or late developmental defects. Brain tumors or cysts are not common causes of cerebral palsy. Internal hydrocephalus following subarachnoid or ventricular blockage may result in spastic forms of cerebral palsy.

Comment.—The clinical importance of the etiological classifications lies in the rather frequently observed association between specific etiological factors and clinical syndromes. This suggests a specificity in the etiological factor that results in a specific pathological and clinical syndrome. Where there is a discrepancy between the history and the expected clinical findings, one would be wise to review both of them, in the hope of finding a clinical correlation.

A generalization of clinical correlation to etiology might be stated as follows: When the etiological factor in cerebral palsy is anoxia or a similar mechanism, the clinical syndromes are those associated with presumably extrapyramidal lesions. In this event, clinically one would expect to find athetoids, rigidities, or tremors. When the etiology is traumatic or vascular in nature, the ensuing clinical syndromes are those that are presumably due to involvement of the pyramidal tracts. In this event, the clinical picture is that of the spastic.

Etiological factors are generally elicited in the clinical history, and clinical syndromes are noted in direct observation of the patient. A more complete correlation between the two is dependent on a better understanding of the morbid anatomic changes that occur in the brain. There is a dearth of factual material in this field, and only further study will help to clarify the enigma of the pathogenesis of cerebral palsy. To this end, the Brain Registry of the American Academy for Cerebral Palsy has already begun to collect brains of cerebral palsy patients who have had reliable clinical histories and clinical observation.

Bearing in mind classifications such as those listed above, one can delineate the various types of cerebral palsy in more descriptive terms. Thus, one may speak of a quadriplegic tension athetoid of mild degree due to anoxia, or of an atonic spastic diplegia of severe degree following premature delivery. Each adjective used implies the definition given in the classification, and thus should have a specific connotation. Although it is recognized that the above classifications may not be the ultimate or final ones, they have been found useful in eliminating some of the confusions in terminology that exist in the field of cerebral palsy.

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Air Swallowing.—All observations support the opinion that external air is the chief source of the gas in gastro-intestinal distention. Ordinary swallowing will take down small amounts of air which with time and some obstruction may produce distention. But large amounts of air can also be inspired into the esophagus voluntarily by individuals able to do air-sucking and by esophageal speech patients, and involuntarily by the nervous aerophagics. This air can travel from the stomach to the cecum in 10 to 15 minutes and be passed as flatus in 30 minutes. . . . We know that increases in the respiratory rate and depth considerably change intra-esophageal negative pressure, and we suspect the nervous reflex mechanism may also alter the superior esophageal sphincter tone or action so that a small amount of air is aspirated into the esophagus with each breath. At a rate of 20 breaths a minute it would not take long for a considerable volume of air to enter the esophagus and stomach.—W. G. Maddock, M.D., Some Observations on Gastro-Intestinal Distention, *Illinois Medical Journal*, December, 1951.

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TERRAMYCIN AND AUREOMYCIN IN SURGICAL INFECTIONS

REPORT OF TWO HUNDRED CASES

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Although other antibiotics have been introduced since penicillin became generally available, it still remains the most widely used of these agents. This might be expected, since it is unsurpassed in the treatment of many bacterial infections, especially those caused by pyogenic cocci. On the other hand, its scope of usefulness is not all-inclusive. Mixed infections respond poorly to penicillin alone. Many strains of staphylococci are penicillin-resistant [1] Some patients cannot tolerate penicillin because of hypersensitivity, a problem which perhaps may be solved by the introduction of penicillin O, although this new product has not yet been fully investigated.[2] Finally, although oral administration would be preferable in the use of antibiotics, the full potentialities of penicillin by this route remain to be established.

The need for an alternative antibiotic agent is therefore clear, and at the present time three possibilities present themselves: (1) chloramphenicol [3] and (2) aureomycin,[4] which are of established value in various staphylococcic and streptococcic infections as well as in gram-negative bacillary, viral, and rickettsial diseases; and (3) terramycin,[5] which has a similar antimicrobial spectrum. The purpose of this communication is to evaluate the results of two of these new agents in 200 surgical infections, 47 of which were treated with aureomycin and the remainder with terramycin.

GENERAL CONSIDERATIONS

Antimicrobial Spectrum.—Most of the 200 infections in this study were caused by pyogenic cocci. In the laboratory of the Brooke Army Hospital Surgical Research Unit [6] a recent survey of 228 strains of staphylococci cultured from as many patients revealed, according to the paper disk method,[7] that 44 of the strains (19%) were resistant to penicillin, 24 (11%) were resistant to terramycin, and 9 (4%) were resistant to aureomycin. Of the 44 penicillin-resistant strains, 38 (86%) were sensitive to terramycin and 40 (91%) were sensitive to aureomycin. Conversely, three-quarters of the terramycin-resistant strains were sensitive to penicillin.

Organisms of the coli-aerogenes group were almost never sensitive to penicillin, but 50 to 60% of 96 were sensitive to both aureomycin and terramycin. In mixed bacterial infections the penicillinase-producing coliform bacilli may inhibit the action of penicillin on penicillin-sensitive organisms. A few strains of proteus vulgaris and pseudomonas aeruginosa were sensitive to both aureomycin and terramycin, but in this group the incidence of chloramphenicol-sensitive strains was much more impressive.

The following facts and possibilities must be borne in mind in the selection of the antibiotic to be used in any given case. Penicillin, as already mentioned, is widely useful in infections caused by pyogenic cocci, though its usefulness may be inhibited in mixed infections in which penicillinase is produced. Terramycin and aureomycin can be used in the great majority of staphylococcic infections, in which penicillin is ineffective, and in the greater proportion of coli-aerogenes infections, in which penicillin is almost never useful. Chloramphenicol is the antibiotic of choice in Proteus vulgaris and Eberthella typhosa infections, in which both terramycin and aureomycin are often ineffective.

Diffusion Into Tissues and Body Fluids.—Much, but not all aureomycin and terramycin is readily absorbed in the blood stream after ingestion. The drugs are excreted in large quantities in the urine, as well as in the feces and exert a suppressive effect on the fecal flora.[8]

Studies by Welch and associates [9] indicate that the serum concentration obtained following comparable single doses of aureomycin and terramycin is approximately the same. Blood concentrations are not materially affected when a single dose of either drug is increased beyond 1.0 gm. These observers found blood levels of 2 to 4 γ per milliliter for six hours after a single oral dose of 1 gm. of terramycin hydrochloride. The levels were slightly higher in 23 patients in our own series who received this dose. With the dosage that we eventually employed (3 gm. initially, followed by 0.5 gm. every six

From the Surgical Research Unit, Brooke Army Hospital, Brooke Army Medical Center, Fort Sam Houston, Texas.

The aureomycin used in this study was supplied by Lederle Laboratories Division, American Cyanamid Company. The terramycin was supplied by Charles Pfizer & Company, Inc.

1. Penicillin-Resistant Staphylococci, editorial, J. A. M. A. **145**: 1268 (April 21) 1951.

2. Volini, I. F.; Shlaes, W. H., and Felsenfeld, O.: Use of Penicillin O in Patients Hypersensitive to Penicillin G., J. A. M. A. **143**: 794 (July 1) 1950.

3. Altemeier, W. A., and Culbertson, W. R.: Chloramphenicol (Chloromycetin®) and Aureomycin in Surgical Infections, J. A. M. A. **145**: 449 (Feb. 17) 1951.

4. (*a*) Finland, M.; Collins, H. S.; Gocke, T. M., and Wells, E. B.: Present Status of Aureomycin Therapy, Ann. Int. Med. **31**: 39 (July) 1949. (*b*) Herrell, W. E.: Observations on the Clinical Use of Aureomycin, Proc. Staff Meet., Mayo Clin. **24**: 612 (Dec. 7) 1949. (*c*) Logan, M. A.; Metzger, W. I.; Wright, L. T.; Prigot, A., and Robinson, E. A.: Aureomycin in Soft Tissue Infections, Am. J. Surg. **79**: 229 (Feb.) 1950; Rutenberg, A. M.; Schweinberg, F. B., and Fine, J.: Clinical Experiences with Aureomycin in Surgical Infections. Ann. Surg. **133**: 344 (March) 1951.

5. Finlay, A. C., and others: Terramycin, a New Antibiotic, Science **111**: 85 (Jan. 27) 1950.

6. It is the custom in this laboratory to test the sensitivity of all organisms encountered to penicillin, streptomycin, aureomycin, terramycin and chloramphenicol, by means of the paper disk method. The commercial preparation of these disks is now under investigation. Antibiotic concentrations of the disks in terms of micrograms per milliliter are as follows: penicillin, 40 γ; streptomycin, 500 γ; aureomycin, 100 γ; terramycin, 100 γ; and chloramphenicol, 1,000 γ.

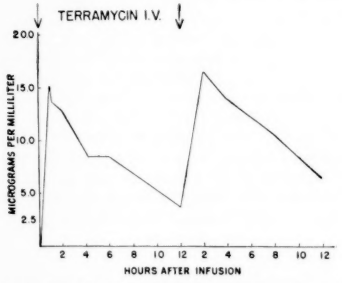
7. Bondi, A., Jr.; Spaulding, E. H.; Smith, D. E., and Dietz, C. C.: A Routine Method for the Rapid Determination of Susceptibility to Penicillin and Other Antibiotics, Am. J. M. Sc. **213**: 221 (Feb.) 1947. Pulaski, E. J.: The Place of Antibiotics in the Field of Surgery, Ann. New York Acad. Sc. **53**: 347 (Sept. 15) 1950.

8. Baker, H. J., and Pulaski, E. J.: Effects of Terramycin on Fecal Flora, Ann. New York Acad. Sc. **53**: 324 (Sept. 15) 1950. Dearing, W. H., and Needham, G. M.: The Effect of Terramycin on the Intestinal Bacterial Flora of Patients Being Prepared for Intestinal Surgery, Proc. Staff Meet., Mayo Clin. **26**: 49 (Jan. 31) 1951.

9. Welch, H.: Absorption, Excretion and Distribution of Terramycin, Ann. New York Acad. Sc. **53**: 253 (Sept. 15) 1950.

hours) blood levels of 4 γ per milliliter were obtained for one to four hours after the initial dose, and levels of approximately 2 γ per milliliter were maintained thereafter. These data are in substantial agreement with those reported by Welch and associates. Adequate therapeutic blood levels can also be obtained by giving terramycin hydrochloride intravenously in 1 gm. doses every 12 hours (see figure).

Herrell and co-workers [10] found no appreciable levels of terramycin in the spinal fluid after giving 1 gm. of the drug every six hours for 24 hours and concluded that terramycin, unlike aureomycin, does not readily traverse the blood-brain barrier. Their investigations, however, were carried out on patients free from meningeal diseases. We found terramycin levels of 3.84 γ per milliliter in the spinal fluid of a patient with meningitis who received 1 gm. of the drug intravenously every 12 hours. The meningitis in this case was secondary to a postpneumonic empyema, and the causative organism, a gamma Streptococcus, was sensitive to terramycin in vitro. The patient recovered from the meningeal infection but died later of a brain abscess. This experience suggests



Terramycin serum levels during intravenous administration of 1 gm. every 12 hours (average of six patients).

that meningeal disease may so alter membrane permeability that terramycin, which cannot pass the normal blood-brain barrier, can enter the spinal fluid in these circumstances.

High concentrations of terramycin have been found in fetal blood and in the pleural fluid.[10] In a case of tuberculous peritonitis with secondary ascites, a concentration of 5 γ per milliliter was obtained in the ascitic fluid. Detailed observations have already been published concerning the diffusion of aureomycin in tissue and body fluid.[11]

Dosage and Route of Administration.—In the early cases in this series aureomycin hydrochloride was administered by mouth in dosages of 0.5 gm. every six hours. When it became evident that a good response was not obtained with this dosage in cases of diffuse cellulitis without abscess formation until 72 or 96 hours had elapsed, the initial dose was increased to 3 gm. Such rapid therapeutic responses were then obtained that this dosage was used in all subsequent cases. Intravenous administration of aureomycin with sodium glycinate was necessary in only two cases. In the first, severe cellulitis of the leg with bacteremia, caused by a nonhemolytic Streptococcus, was accompanied by such severe vomiting that medication by mouth was not possible. Twelve hours after the administration of the intravenous dose (0.5 gm. in 250 cc. of 5% dextrose solution) a single dose of 2.5 gm. was given by the oral route and was retained. The second patient required intravenous therapy because of dysphagia caused by a large submandibular abscess. After three days of twice-daily medication by this route the infection subsided sufficiently to permit oral administration of the drug.

TABLE 1.—*Results in Forty-Seven Patients with Soft Tissue Infections Treated with Aureomycin*

Diagnosis	No. of Cases	Response		
		Good	Doubtful	None
Cellulitis	30	23	6 *	1 †
Cellulitis with early abscess	10	7	2 *	1 †
Furunculosis	3	2	1 ‡	0
Postpartum mastitis	4	3	1 §	0
Total	47	35	10	2

* Drug discontinued because of intolerance.
† Probably caused by inadequate dosage.
‡ Probably caused by low initial dose.
§ Possibly caused by interference with absorption by aluminum hydroxide.

The experience with aureomycin suggested a similar dosage for terramycin hydrochloride. It was therefore given in most cases in this series in an initial dose of 3 gm. followed by 0.5 gm. every six hours. In five cases in which the intravenous route was substituted for the oral route, 1 gm. was administered in 500 cc. of 5% dextrose solution; the infusion was run in as rapidly as was consistent with safety.

Untoward Reactions.—There were 9 instances of untoward reactions to aureomycin in the 47 patients treated with this drug. Two patients experienced such intractable vomiting that the drug had to be withdrawn; in both cases vomiting began after the initial administration of 3 gm. Another patient had urticaria of the face after the first dose. The reaction responded promptly to antihistaminic therapy, and there was no recurrence when aureomycin was continued. In the other six patients the reactions were not severe. Four patients experienced nausea, and two had frequent bulky stools. Our experience thus duplicates that of others and indicates that untoward

TABLE 2.—*Cellulitis (Forty-One Patients) Treated with Terramycin*

Diagnosis	No. of Patients	Days of Treatment	Results		
			Excellent	Good	Doubtful
Cellulitis					
Closed infection	18	5.8	6	12	..
Cellulitis without Abscess					
Hemolytic Staph. aureus	3	7	2	..	1
Hemolytic Streptococcus	3	7	2	1	..
Esch. coli	1	12	1	..	..
Cellulitis with Abscess					
Hemolytic Staph. aureus	8	7	2	6	..
Hemolytic Streptococcus	4	4.5	1	3	..
No culture obtained	4	4	2	2	..

10. Herrell, W. E.; Heilman, F. R.; Wellman, W. E., and Bartholomew, L. G.: Terramycin: Some Pharmacologic and Clinical Observations, Proc. Staff Meet., Mayo Clin. **25**: 183 (April 12) 1950.

11. Herrell, W. E., and Heilman, F. R.: Aureomycin: Studies on Absorption, Diffusion and Excretion, Proc. Staff Meet., Mayo Clin. **24**: 157 (March 30) 1949.

reactions following the oral use of aureomycin are seldom severe enough to contraindicate its continued administration. It has been found that patients who do not tolerate the large initial dose can be given the drug intravenously, after which frequent smaller doses can be given by the oral route.

Terramycin is apparently free from serious toxic properties. In 153 patients there were 6 instances of nausea and vomiting, 10 of diarrhea, and 1 of proctitis; but all were mild. Several other patients complained of burning epigastric pain during the course of therapy. A few patients in the group treated for peritonitis had intractable nausea and vomiting after intravenous administration. In no case in either series were nephrotoxicity or hemopoietic disturbances noted, there being no deviations from the normal in the repeated urinalyses and blood cell counts carried out during treatment.

AUREOMYCIN

Results were satisfactory in 35 of the 47 infections in which aureomycin was used (Table 1), and the doubtful responses and failures were readily explained. In both failures, therapy had to be discontinued because of drug intolerance, as evidenced by uncontrolled nausea and vomiting. In the 10 instances of doubtful response, the 8 patients with cellulitis received doses that were probably insufficient, while the patient with furunculosis probably had an inadequate initial dose. The remaining patient in this group, who had postpartum mastitis, probably did not receive the full benefit of the aureomycin because, as has since been learned, the simultaneous administration of aluminum hydroxide interfered with its absorption.[12] Our general experience thus corresponds with the experience of others who have used aureomycin for similar infections.[4c]

TERRAMYCIN

Cellulitis.—There were no failures of treatment in the 41 cases of cellulitis treated with terramycin (Table 2), although 5 patients had infections of such severity that intravenous medication was required. The single patient whose response was doubtful had an infecting organism that was only slightly sensitive to terramycin in vitro. The response in 16 cases was classified as excellent in that dramatic clinical improvement was observed in 24 to 48 hours, as manifested by a fall in the temperature, a decrease in the leukocyte count, regression of the lesion, and improvement in general appearance of the patient. Twenty-four responses were classified as good, meaning that there was a gradual, steady clinical improvement over periods ranging from three to seven days. In 11 of the 16 cases with abscess, incision and drainage were employed, and in 2 others the abscess was aspirated and the cavity filled with terramycin. This means that in 13 of the 16 cases some surgical measure was combined with the antibiotic therapy. Beneficial effects of treatment, therefore, cannot be ascribed specifically to one form of therapy or the other. In many instances, however, terramycin appeared to hasten localization of the infectious process and to reduce the area of cellulitis surrounding the abscess, which suggests that most of the good results in this group can be attributed to the combined treatment.

Bacteremia.—Five of six patients with bacteremia (Table 3) had excellent results, as manifested by prompt clinical improvement, fall in temperature, and sterilization of the blood stream. All were treated by the intravenous route. One patient received aureomycin, and five patients received terramycin. In one case, that of a patient with 57% full-thickness burn and hemolytic streptococcic bacteremia, terramycin treatment was a complete failure. The organism was resistant to all the common antibiotics, and the patient died of an overwhelming septicemia. In one instance (Case 2) only a single dose of terramycin was administered intravenously. This is probably insufficient for a blood stream infection, as shown by the fact that it was 72 hours before the patient became afebrile. In the other patients treated with terramycin, intravenous medication was continued for two or three days, and resolution was correspondingly more rapid.

TABLE 3.—*Bacteremia Treated with Aureomycin and Terramycin*

Case No.	Infecting Organism	Primary Disease	Antibiotic Used	Days of Treatment	Results
1*	Nonhemolytic Streptococcus	Cellulitis of foot	Aureomycin	8	Excellent, afebrile in 72 hours
2	Str. viridans	Cellulitis of leg	Terramycin	10	Excellent, afebrile in 72 hours
3	Hemolytic Staph. aureus	Unknown	Terramycin	15	Excellent, afebrile in 48 hours
4	Hemolytic Streptococcus	Osteomyelitis of tibia	Terramycin	6	Excellent, afebrile in 36 hours
5	Hemolytic Streptococcus	Full thickness burn	Terramycin	8	Failure, patient died of overwhelming septicemia
6	Hemolytic Streptococcus; Esch. coli	Infected gunshot wound of abdomen	Terramycin	9	Excellent, afebrile in 48 hours. Previous chloramphenicol, streptomycin, and penicillin therapy failed

* Also included in Table 1.

Miscellaneous Surgical Infections.—Four cases of gas gangrene of the leg were treated by emergency amputation and terramycin. The results were excellent in two patients, whose temperatures fell from 104 F to normal within 36 hours after amputation and institution of terramycin therapy. In the other two patients a less dramatic decline of the temperature was seen, but the response was good, as evidenced by the regression of symptoms in three days. Excellent results were obtained in three patients with anerobic clostridial cellulitis. As soon as the diagnosis was established the patients were given terramycin intravenously, and wide surgical excision of all devitalized tissue was done.

12. Seed, J. C., and Wilson, C. E.: The Effect of Aluminum Hydroxide on Serum Aureomycin Concentrations After Simultaneous Oral Administration, Bull. Johns Hopkins Hosp. **86**: 415 (June) 1950.

The two cases of actinomycosis are worth reporting in detail.

A 45-year-old white man with a history of intermittent swelling in the left parotid area for nine months was hospitalized because a recurrence five weeks before had persisted and, for the first time, was painful. Examination revealed a round, tender mass located at the lower anterior border of the left parotid gland and fixed to the skin. Aspiration produced 5 cc. of thick, greenish, purulent material. Culture was positive for Actinomyces bovis, which was sensitive to terramycin. The administration of penicillin procaine in 600 000 unit doses twice daily for eight days produced no improvement. Terramycin hydrochloride was then administered concurrently, in daily doses of 3 gm. At the end of three days of combined treatment the mass had decreased in size, and the dosage of terramycin hydrochloride was reduced to 2 gm. daily. Combined treatment was continued for a total of 14 days. At the end of this time only a very small, nontender nodule remained at the site of the original lesion. It was excised six weeks later, and there has been no recurrence in the nine-month period which has elapsed.

TABLE 4.—*Miscellaneous Surgical Infections (Fifty-One Patients) Treated with Terramycin*

No. of Patients	Diagnosis	Days of Treatment	Results			
			Excellent	Good	Doubtful	No Response
4*	Gas gangrene of leg (Cl. welchii)	8	2	2	..	..
3†	Anaerobic (Cl. welchii) cellulitis	8.1	3	..	..	..
2	Actinomycosis of jaw	14	2	..	..	..
	Infected traumatic wounds					
5	Hemolytic Staph. aureus	5.4	1	3	1	..
4	Hemolytic Streptococcus	5.4	2	2	..	..
2	Coli-aerogenes group	5.4	..	1	1	..
1	Pseudomonas	5.4	..	..	1	..
1	Klebsiella	5.4	..	1	..	..
3	No culture obtained	5.4	1	2	..	..
10	Infected burn granulations	11.3	..	..	..	10
3	Acute osteomyelitis	15	1	2	..	..
8	Furuncles and carbuncles	5	2	6	..	..
1	Human bite of hand	5	1	..	..	..
1	Dog bite of leg	4	1	..	..	..
1	Sting ray bite of foot	5	..	1	..	..
1	Acute parotitis (Hem. Streptococcus)	13	1	..	..	..
1	Breast abscess (Hem. Staphylococcus)	8	..	1	..	..

* Amputation in all four.
† Wide incision in all cases.

A 21-year-old man was hospitalized because of a painful swelling below the angle of the jaw, which had been present for six weeks prior to admission. He had received 300,000 units of penicillin procaine daily for seven days elsewhere, without evident results. Examination revealed a fluctuant mass, 5 by 5 cm., posterior and inferior to the angle of the right mandible. When it was incised, a large amount of purulent material exuded. This material yielded sulfur granules, but the culture was inadvertently misplaced before sensitivity tests could be obtained. Drainage ceased after five days of oral terramycin therapy, but treatment was continued for an additional nine days. The patient left the hospital with a well-healed wound.

Both of these cases illustrate an excellent response to terramycin after penicillin had been given without effect. Penicillin was continued in the first case, in which the results must be attributed to combined therapy, but not in the second, in which terramycin alone was responsible for the good results. The successful management of cervical actinomycosis with combined sulfonamide-penicillin therapy has been previously reported, and the first of the above cases suggests that a combination of terramycin and penicillin may be equally successful.

The results in 16 infected traumatic wounds were excellent in 4, good in 9, and doubtful in 3. One case was of particular interest because it demonstrated the necessity for adequate dosage of terramycin over a sufficient period of time. This patient had a traumatic ulcer surrounded by an area of cellulitis on the dorsum of the foot. Within 24 hours of the institution of treatment the temperature fell from 102.6 F to normal, and the surrounding erythema completely disappeared. By the end of the fifth day the ulcer was completely healed. Because diarrhea had occurred during therapy, the dosage was reduced from 0.5 gm. to 0.25 gm. every six hours. Three weeks later the cellulitis recurred. The same organism, a beta hemolytic Streptococcus, was again isolated. The infection responded within 48 hours to the administration of 0.5 gm. of terramycin hydrochloride every six hours. Treatment was continued for six days, and there were no further recurrences. The three cases showing doubtful response were infected gunshot wounds. In one patient the offending organism was a hemolytic Staphylococcus aureus, not sensitive to terramycin; in another Pseudomonas, and in the third, a coliform bacillus.

Ten patients with infected burn granulations received terramycin for an average of 11.3 days. In no instance did terramycin therapy influence the patient's course, the appearance of the granulation tissue, or its microbial flora. The infecting organisms were sensitive to terramycin in vitro in six cases and resistant in four, but the results were equally poor in all. The clinical picture remained unaltered irrespective of the degree of in vitro sensitivity.

Two of the three patients with acute osteomyelitis showed a good response and the other an excellent response to terramycin therapy. The last-mentioned patient had acute hematogenous osteomyelitis. In one of the other cases the osteomyelitis was secondary to a large subcutaneous abscess of the thigh, which was not evacuated for three weeks.

Results from terramycin therapy were excellent in two patients with furunculosis. A good response was obtained in four other patients with furuncles and two with carbuncles. In one patient, a large furuncle on the upper lip, which had not responded to 3,000,000 units of penicillin procaine, required surgical drainage. When the patient was first seen, the lesion was indurated. Localization was complete within 24 hours of the first dose of terramycin, and healing was uneventful after surgical drainage. The two patients with carbuncles received terramycin as an adjunct to surgical drainage and débridement.

In a patient with a human bite infection of the index finger, tenderness and edema disappeared within 72 hours. Acute pyogenic parotitis due to hemolytic Streptococcus that had not responded to penicillin and x-ray therapy subsided after 10 days of treatment with terramycin.

Peritonitis.—Fifty-six patients with acute secondary peritonitis following appendicitis, penetrating gunshot wounds of the abdomen, and other causes were treated with terramycin (Table 5). The diagnosis of spreading peritonitis was made in those patients with marked ileus, distention, diffuse abdominal tenderness, high fever, and toxemia. The temperature response, reappearance of

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peristalsis, and subjective sense of improvement of the patient were used as guides in the evaluation of therapy. Seventeen of the 27 patients with spreading peritonitis showed excellent results from terramycin treatment, as evidenced by a fall in temperature to normal in 48 to 96 hours and a return of peristalsis in 48 hours. In six patients good results were obtained after four to five days of therapy. There were four treatment failures. All were patients with peritonitis secondary to perforating gunshot wounds. In all instances cultures of peritoneal exudate showed organisms resistant to terramycin (staphylococci, nonhemolytic streptococci and/or coliform bacilli). After 48 to 72 hours of intravenous administration of terramycin with no change in the condition of the patient, another antibiotic to which the cultured bacteria were sensitive was given. Subsequently, all four patients progressed to an uneventful recovery.

Results in 13 patients with localizing peritonitis of appendical origin treated with surgery and terramycin were gratifying. Ten patients with localized peritonitis were treated with surgical drainage and terramycin. The exact role of the antibiotic as an adjunct to surgery is difficult to evaluate. Acute exacerbation of pelvic inflammatory disease was promptly controlled by terramycin in six patients, but no significant changes in the size of the pelvic masses were detectable. This experience with human peritonitis confirms our previous data [13] in experimental peritonitis and shows the therapeutic efficacy of this antibiotic in peritoneal infections.

COMMENT

The multiplicity of factors involved in the uneventful resolution of a surgical infectious process makes it difficult to evaluate the role played by whatever antibiotic may be used in treatment. Moreover, the small number of patients in this series makes it impossible to draw any statistically significant conclusions. On the other hand, certain definite clinical impressions seem justified. Aureomycin and terramycin are clearly useful agents in surgical infections. They are superior to penicillin in at least two respects: their wider antimicrobial spectra and their convenient administration by the oral route without loss of effectiveness and without serious untoward reactions. Furthermore, allergy and drug-fastness are as yet minor problems with them.

However, experience with penicillin in pyogenic surgical infections on a large scale has been so satisfactory that penicillin will not easily be displaced as the drug of choice in these infections. Terramycin and aureomycin must be studied much more intensively before any final judgment is passed on their role in the surgeon's therapeutic armamentarium. For the present, it can be said that they are undoubtedly useful alternates in the antibiotic treatment of soft tissue infections. The practitioner who does not have ready access to laboratory facilities, when confronted with an acute pyogenic infection that fails to respond to penicillin in 24 to 48 hours, can safely use either terramycin or aureomycin with an 85 to 90% assurance that treatment will be effective.

Mixed infections offer the most promising field of usefulness for the newer antibiotics. Combined therapy with penicillin and streptomycin has already achieved excellent results in mixed gram-positive coccic and gram-negative bacillary infections.[14] If a single orally-administered drug can replace two drugs that must be administered by the parenteral route, the advantage is self evident. Both aureomycin and terramycin have been shown to give very promising results in the treatment of peritonitis.[15]

In many of the patients in this series good results were achieved by a combination of antibiotic treatment and surgical drainage. In all probability, good results could have been obtained in some of these patients by immobilization and surgery alone, but adjuvant specific therapy is thought to have expedited cure. Other cases show that antibiotic therapy has not eliminated the necessity for surgical drainage of well-formed abscesses.

Terramycin and aureomycin are similar in their antimicrobial spectra, dosage, route of administration, and seemingly, in the mechanism of their antibacterial action. Both are bacteriostatic rather than bactericidal. Herein lies their inferiority to penicillin, which, if given in very high dosages, is predominantly bactericidal. Consequently, in diseases such as endocarditis, in which a cure depends on the actual destruction of bacteria, results of treatment with aureomycin have not been encouraging.[14a] Similarly, a high recurrence rate has been observed in brucellosis, unless an adequate dosage has been given for a prolonged period of time. These experiences, translated to surgical infections, suggest the need for sufficiently high dosages and for therapy of proper duration.

TABLE 5.—*Peritonitis Treated with Terramycin* *

Type	Total Cases	Response: Excellent	Good	Poor	Doubtful
Spreading peritonitis †	27	17	6	4 ‡	..
Localizing peritonitis	13	6	7	..	..
Localized peritonitis	10	1	3	2	4
Pelvic inflammatory disease	6	..	6	..	..
Total	56	24	22	6	4

* Dose: 1 gm. intravenously twice daily for 3 to 4 days, then 2 gm. orally for 10 days.
† Appendicitis, 6; gunshot wound, 14; perforated viscus, 3; knife, bowel resection, intestinal strangulation, unknown, 1 each.
‡ Gunshot wound.

SUMMARY

A report is made on 47 patients with surgical infections treated with aureomycin and 153 patients treated with terramycin. Of the 47 aureomycin-treated patients, results were unsatisfactory in only 12, the reasons for the poor response being evident. The results in the remaining 35 patients were satisfactory. All but one of the 41 patients with cellulitis treated with terramycin exhibited

13. Pulaski, E. J.; Shaeffer, J. R.; Artz, C. P., and Baker, H. J.: Studies on the Use of Terramycin in Experimental and Clinical Peritonitis, in Surgical Forum: 1950 Clinical Congress of the American College of Surgeons, Philadelphia, W. B. Saunders Company, 1951, pp. 119-128.

14. (*a*) Herrell, W. E., in discussion of Symposium on Antibiotics before the Joint Meeting of the Section on Internal Medicine and the Section on Experimental Medicine and Therapeutics at the Ninety-Ninth Annual Session of the American Medical Association, San Francisco, June 30, 1950, J. A. M. A. **144**: 533 (Oct. 14) 1950. (*b*) Jawetz, E.; Gunnison, J. B., and Coleman, V. R.: The Combined Action of Penicillin with Streptomycin or Chloromycetin on Enterococci in vitro, Science **111**: 254 (March 10) 1950. (*c*) Pulaski, E. J., and Baker, H. J.: Combined Therapy of Infectious Disease, South. M. J. **42**: 765 (Sept.) 1949.

15. (*a*) Pulaski and associates.[15] (*b*) Wright, L. T., and Prigot, A.: Aureomycin as an Aid in Abdominal Surgery, Ann. Surg. **133**: 364 (March) 1951.

gratifying results. An excellent response was evident in four of the five cases of terramycin-treated bacteremia. Satisfactory results were obtained in almost all of the group of 51 miscellaneous surgical infections. Ten patients with extensive infected burns failed to respond. The excellent results recorded in 52 of 56 patients with peritonitis suggest the value of terramycin in this type of infection. The four treatment failures in this group are attributed to the fact that organisms resistant in vitro to terramycin were present.

COORDINATED APPROACH TO ANTABUSE® THERAPY

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So disappointing have been the drugs and methods used in the approach to the problem of alcoholism that one must exert great caution in evaluating any new technique. However, recently many enthusiastic reports have entered the literature concerning the drug known as tetraethylthiuramdisulfide, or, as it is more commonly called, antabuse.[*1]

From the historical background, it has been noted previously that workers exposed to tetraethylthiuramdisulfide in the rubber industry had discovered their tolerance for alcohol considerably decreased. Hald and Jacobsen [2] employed tetraethylthiuramdisulfide as a possible anthelmintic and found that there were no toxic effects over an extended period of time. They also observed that contact with alcohol produced a moderately severe disagreeable physical reaction, consisting of headache, flushing, palpitation, nausea, and vomiting. The physical effects were explained on the basis of the drug's interference with the metabolism of alcohol at the acetaldehyde stage, allowing acetaldehyde to accumulate. Voegtlin's [3] studies with the conditioned reflex emetine aversion method indirectly suggested the possibility of using tetraethylthiuramdisulfide as a pure aversion technique. Martensen-Larsen [4] described the clinical results in 1948, indicating its favorable effect.

Our purpose in presenting this paper is to report the studies and results on a series of 32 chronic addictive drinkers over a period of eight months at the Blue Hills Clinic,[5] Hartford, Conn. Our previous study [6] has dealt with the preliminary psychiatric implications of tetraethylthiuramdisulfide. This paper intends to incorporate some of these findings and to correlate them with the over-all medical and physiological implications.

SELECTION OF PATIENTS

Because of the severe physical reactions that can occur during the tetraethylthiuramdisulfide-alcohol reaction, it has been our belief that only hospitalized patients should be started on the drug. Patients are selected after a thorough screening process, which consists of three parts: (1) complete physical examination, (2) neuropsychiatric survey, and (3) laboratory studies.

The Danish workers have stressed certain physical conditions that preclude the administration of tetraethylthiuramdisulfide. These investigators [7] have felt that the presence of severe degrees of myocardial disease or failure, hypertension, diabetes mellitus, hypothyroidism, hyperthyroidism, epilepsy, nephritis, cirrhosis of the liver, pregnancy, and paraldehyde addiction were definite contraindications. The outstanding physical phenomenon in the tetraethylthiuramdisulfide-alcohol reaction is most commonly a circulatory one, and in the evaluation of a patient from a physical point of view, a sound cardiac status is desirable. The cardiac examination of the patient is thus detailed and includes the resting electrocardiogram and a Two-Step Master Test.[8] Hypertension of moderate degree without cardiac abnormalities and diabetes mellitus have not presented absolute contraindications in our experience. In addition, the presence of a cirrhotic process in the liver has not presented an absolute barrier to the introduction of tetraethylthiuramdisulfide. The degree of liver dysfunction as demonstrated by laboratory testing must be evaluated in an absolute sense and in the light of future damage caused by continued alcoholic excess.

The potential effects of tetraethylthiuramdisulfide should be carefully evaluated from the psychiatric viewpoint. Reports of personality disorganization have been observed by many investigators.[9] Thus, the understanding of the psychodynamics in the patient receiving the drug is important. We believe that tetraethylthiuramdisulfide in its representation of help may act in two different directions: first, it may reinforce the existing

Drs. Leon Greenberg and David Lester assisted in the laboratory and physiological studies, and technical aid was given by Mr. Morris Freidman.

Associate Physicians, Internal Medicine (Drs. Mann and Conway); Physician-in-Charge, Outpatient Service (Dr. Gottesfeld); and Physician-in-Charge, Inpatient Service (Dr. Lasser); Blue Hills Clinic.

1. Antabuse® was supplied for research purposes by Ayerst, McKenna and Harrison, Ltd., New York.

2. Hald, J., and Jacobsen, E.: A Drug Sensitizing the Organism to Ethyl Alcohol, Lancet **2**: 1001-1004 (Dec. 25) 1948.

3. Voegtlin, W. L., and Broz, W. R.: The Conditioned Reflex Treatment of Chronic Alcoholism; Analysis of 3,125 Admissions Over a Period of 10½ Years, Ann. Int. Med. **30**: 580-597 (March) 1949.

4. Martensen-Larsen, O.: Treatment of Alcoholism with a Sensitizing Drug, Lancet **2**: 1004-1005 (Dec. 25) 1948.

5. The clinic is operated by the State of Connecticut under the Commission on Alcoholism and has been in operation since April, 1950. It is composed of both an outpatient department and an inpatient department, the latter having 50 beds.

6. Gottesfeld, B. H.; Lasser, L. M.; Conway, E. J., and Mann, N. M.: Psychiatric Implications of the Treatment of Alcoholism with Tetraethylthiuram Disulfide; Preliminary Report, Quart. J. Stud. Alcohol **12**: 184-205 (June) 1951.

7. Glud, E.: The Treatment of Alcoholic Patients in Denmark with "Antabuse," with Suggestions for Its Trial in the United States, Quart. J. Stud. Alcohol **10**: 185-197 (Sept.) 1949.

8. Master, A. M.; Friedman, R., and Dack, S.: The Electrocardiogram After Standard Exercise as a Functional Test of the Heart, Am. Heart J. **24**: 777-793 (Dec.) 1942.

9. (*a*) Gottesfeld, Lasser, Conway, and Mann.[6] (*b*) Bennett, A. E.; McKeever, L. G., and Turk, R. E.: Psychotic Reactions During Tetraethylthiuramdisulfide (Antabuse) Therapy, J. A. M. A. **145**: 483-484 (Feb. 17) 1951. (*c*) Bowman, K. M., and others: A Clinical Evaluation of Tetraethylthiuramdisulfide (Antabuse) in the Treatment of Problem Drinkers, Am. J. Psychiat. **107**: 832-838 (May) 1951

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therapeutic relationship to the individual physician, psychotherapist, group, or hospital; second, it may unconsciously represent a type of threat which being equated with psychotherapy and its implications may arouse such ambivalence that therapy is terminated.

Examination of the life history pattern will give important indications of the anticipated reaction to therapy and tetraethylthiuramdisulfide. Persons who have had the most traumatic experiences in childhood with parental figures will, as a rule, find it increasingly difficult to adjust to therapeutic figures who act as parental substitutes. The ability of the patient to accept and respond to help is not necessarily based on conscious mechanisms; thus many who have initially appeared eager for a solution to their problems have been prominent failures.

To such threatened persons, tetraethylthiuramdisulfide and the implications of sobriety and therapy can represent a stress that forces them to utilize a "last ditch" defense measure, the psychotic or near-psychotic reaction. In our experience, those who have become disorganized have been borderline schizophrenic and schizoid persons. The overt schizophrenic has not been considered for tetraethylthiuramdisulfide therapy. Under intense stress some of the patients in the former group are known to have shown transient but marked personality disturbances in their past lives.

It is important to recognize, nevertheless, that all borderline schizophrenics will not become disorganized during the course of therapy. The crucial factors responsible for the ability to remain intact appear in most instances to be the absence of highly organized projective and sadomasochistic difficulties along with the ability to maintain some control over hostile, aggressive impulses. In the last analysis the adjustment to therapy and tetraethylthiuramdisulfide depends on the dynamic adjustment of the patient, his present interpersonal and object relationships, and his past and present reactions to help and to stress. It is possible that toxic factors may contribute to the disorganization, but the expression of the breakdown appears to depend on dynamic considerations.

The laboratory examinations required include (1) complete blood cell count, (2) urinalysis (with renal function tests where indicated), (3) Wassermann test, (4) nonprotein nitrogen determination, (5) fasting blood sugar test, (6) cephalin flocculation, (7) sulfobromophthalein sodium test, and (8) electrocardiogram. Further studies, such as chest x-ray, electroencephalogram, and basal metabolism test, are done where indicated.

ROUTINE

Tetraethylthiuramdisulfide is not administered at the clinic to patients under the effects of a recent alcoholic debauch. This is felt to be a dangerous practice, inasmuch as the subject under observation is an unknown with respect to tetraethylthiuramdisulfide reactivity. Individuals vary in their reactions to the combination of tetraethylthiuramdisulfide and alcohol. Thus, it would be unwise to administer tetraethylthiuramdisulfide to one whose blood alcohol level was already elevated in the absence of a previous controlled test.

We have been accustomed in our earlier cases to using the tetraethylthiuramdisulfide dosage routine suggested by Glud.[7] This has consisted essentially of the administration of 2 gm. on the first day, 1.5 gm. on the second day, 1 gm. on the third day, and 0.75 gm. on the fourth day. On the last day, the test reaction with alcohol is given. The dose of actual alcohol employed is usually 10 to 14 cc. in the form chosen by the patient. The subject is carefully supervised throughout the entire reaction by a staff that includes physicians, nurse, and attendant. A tetraethylthiuramdisulfide emergency truck, containing oxygen, cardiac and respiratory stimulants, intravenous ferrous ascorbate and vitamin C, and intravenous fluids, is kept constantly on hand for any untoward situation. After the initial reaction, the dosage is decreased to a maintenance dose varying from 0.25 to 0.75 gm. each day and subsequent reactions are held periodically for reinforcement purposes.

Recently, we have begun to calculate dosage of tetraethylthiuramdisulfide on the basis of body weight. It has been apparent for some time that some attempt should be made to calculate dosage with relation to the weight of the individual patient. Therefore, studies were made, and are still in progress, whereby an initial daily priming dose of 20 mg. per kilogram of body weight is employed. This project is under investigation in order to establish a more consistent approach to the subject of dosage. Emotional factors, constitution, and toxicity may play a definite role, but this has not been completely evaluated.

TABLE 1.—*Psychiatric Classification of Patients*

Neurotic Character Disorder, Case No.	Borderline Schizophrenia, Case No.	Paranoid Condition, Case No.
1* 3 4*	2 7 9	12 17
5* 6 8*	10 14 18	
11 13 15	22 23 24	
16 19* 20		
21* 25 26		
27* 28* 29		
30* 31* 32*		

* With schizoid trends.

The following material deals with detailed studies carried out thus far on 32 addictive alcoholics. From a purely somatic point of view, it may be noted that four of these patients had moderate hypertension. One of the patients had accompanying cardiac enlargement with a normal resting electrocardiogram but a positive Two-step Master Test. This patient, however, had no clinical angina or history of decompensation. Tetraethylthiuramdisulfide was given with recognition of the risk to a patient whose course with her alcoholic history would otherwise have been precarious. One patient exhibited mild diabetes mellitus regulated by diet. Another patient exhibited an enlarged liver, although hepatic function tests were not adversely affected.

The psychiatric evaluation of the above series of cases is presented in Table 1. The survey of a potential tetraethylthiuramdisulfide candidate makes use of a battery of psychological tests, including the Rorschach. The services of the social service department are considered invaluable in estimating the patient's adaptation to his family and community and in helping to evaluate his life-long mode of emotional response.

It will be noted in Table 1 that by far the greatest number of cases fall into the neurotic group. It is em-

phasized that the evaluation as given above represents our conception of the patients prior to the institution of the tetraethylthiuramdisulfide regimen. This proved to be correct in our subsequent experience except in one case (Case 26), where the extreme degree of defensive orientation served to mask the underlying schizoid mechanisms.

TETRAETHYLTHIURAMDISULFIDE-ALCOHOL REACTION

The effects of the tetraethylthiuramdisulfide-alcohol reaction have been described as formidable. These consist of manifestations primarily of a circulatory type, although respiratory and gastrointestinal signs are also prominent. Flushing of the skin, cyanosis, dyspnea, vomiting, tachycardia, and occasional severe falls in blood pressure are features that are all common and have been emphasized previously. In the group under study the erythema described as so outstanding in other writings was seen in all patients; 18% experienced dyspnea; 75% complained of nausea; 63% had vomiting; 12% reported abdominal cramps; and 85% passed into a deep slumber after their reactions.

TABLE 2.—*Side-Effects* to Tetraethylthiuramdisulfide*

Case No.	Drowsiness	Nausea	Abdominal Cramps	Sexual Drive	Hives	Psychotic Reactions
1	+	0	0	↓	0	0
2	0	0	0	↑	0	0
3	+	+	0	↑	0	0
4	+	0	0	↓	0	+
5	+	0	0	—	0	0
6	+	0	+	↑	0	+
7	+	0	+	↑	0	+
8	+	0	0	↑	0	0
9	+	0	+	↑	0	+
10	0	0	0	—	0	0
11	+	0	0	↑	0	0
12	+	0	+	↓	0	+
13	+	0	0	—	0	0
14	+	0	+	—	0	0
15	+	0	0	—	0	0
16	+	0	+	↑	0	0
17	+	0	0	—	0	0
18	+	0	0	↓	0	+
19	+	0	0	↓	0	0
20	+	0	0	—	0	0
21	+	+	0	↑	+	0
22	+	0	+	—	0	0
23	0	0	0	↑	0	0
24	+	+	+	—	0	0
25	—	0	+	—	0	0
26	0	0	0	—	0	+
27	+	0	0	—	0	0
28	+	0	+	—	0	0
29	+	0	0	↑	0	0
30	+	+	+	—	0	+
31	+	0	+	—	0	0
32	+	0	+	—	0	0

* Present +; absent 0; no change —; increased ↑; decreased ↓.

Marked disturbances of blood pressure, pulse and respiratory rate recordings were evident. Seen rather early was a marked increase in pulse rate, accompanied later by a moderate drop in systolic pressure and an even severer decrease in diastolic pressure. The respiratory excursions were frequently increased in rate and at times became labored.

In several cases the vasomotor responses were so severe that falls of 40 to 50 mm. in the systolic pressure were noted; levels in the diastolic pressure of 20 to 40 mm. not infrequently accompanied this phenomenon. Despite these striking features, the patient's condition in most instances was not alarming. Under careful observation, the unusual changes were seen to regress as the reaction waned in its intensity. In one case (23), however, the ensuing reaction proved so severe, that emergency aid was found necessary. This patient had not exhibited a satisfactory reaction on his first test with standard doses of alcohol. Because of the patient's particularly flat emotional response to the test and inasmuch as a good reaction was desirable from a therapeutic standpoint, a larger amount of alcohol was ordered for the second test—55 cc. of whiskey was given. The patient subsequently became very ill, exhibiting marked cyanosis, cardiac extrasystoles, and eventual shock. Oxygen, elevation of the foot of the bed, and cardiac stimulants were administered, with eventual satisfactory results. While ferrous ascorbate and vitamin C used intravenously have been reported as satisfactory antidotes for this type of reaction, our use of this medication in alarming situations and also in preliminary controlled tests has not resulted in the success claimed by others.[10] These experimental tests are continuing. The most reliable and effective aids to date in the extremely severe reaction have been oxygen administered by nasal catheter, the occasional administration of intravenous fluids, such as 5% dextrose in isotonic sodium chloride solution, use of the Trendelenberg position where necessary, and the occasional administration of such stimulants as caffeine sodium benzoate and epinephrine.

Painstaking cardiac examination prior to the acceptance of a patient for tetraethylthiuramdisulfide therapy has been stressed previously, but periodic checks of the cardiac mechanism during the actual reactions is also important. It has been our custom usually to test each patient electrocardiographically at the height of the reaction. Of 24 patients tested in the present group, all exhibited an increased rate but no significant disturbance of rhythm. Fifty-four per cent revealed depression of the S-T segments in various leads, and 92% showed T wave changes varying from lowering of amplitude to actual inversion. These alterations are usually quickly reversible. However, the danger of an acute irreversible cardiac insult is to be kept in mind, particularly when dealing with members in the older age groups.

SIDE-REACTIONS TO TETRAETHYLTHIURAMDISULFIDE

While initially the lack of any side reactions to tetraethylthiuramdisulfide taken over a long period of time was stressed, definite side-effects have since been noted. Prominent among these have been drowsiness, nausea, abdominal cramps, and diminished sexual drive. These have been listed in Table 2. It will be noted that almost 90% of the group complained of drowsiness. This, at times, became rather annoying to the patient, especially during his working hours. Patients awaiting their therapeutic interviews would on occasion be found sleeping in the reception room. This effect in many cases proved beneficial, as it was accompanied by loss of anxiety and tension. In most subjects, the sedative action was transient, lasting only two to five weeks after institution of therapy.

10. Jokivartio, E.: Effect of Iron Preparations on "Antabuse"-Alcohol Toxicosis, Quart. J. Stud. Alcohol **11**: 183-189 (June) 1950.

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Occasionally, nausea and abdominal cramping pains persisted for many days after the tetraethylthiuramdisulfide-alcohol reactions. In four subjects, nausea continued to be a disturbing factor for a period of approximately one month. Abdominal discomfort was a more prominent side-effect; 40% of the series complained for a period of three to four weeks after discharge. In many instances, it was necessary to lower the maintenance dose for a short period and institute therapy of an antacid and antispasmodic nature.

In half of the series, some alteration of sexual drive was observed in the early phase following discharge from the clinic and during outpatient care. Thirty-four per cent revealed increased sexual vigor and drive, although all except one patient (Case 12) indicated difficulty in achieving orgasm. Sixteen per cent reported a decrease in sexual drive and potentia.

A manifestation of this nature is very disturbing to the patient. Sexual prowess in the male in our society is considered a criterion of masculine function. As such, it is an important factor to consider, especially in dealing with disturbed persons. This was a trying element in the therapeutic interviews. Fortunately, the effect was transient in most cases. Much discussion has centered about the possibility that this effect is physiological in origin. We feel that physiological factors should be considered as only a part of the total picture and that these sexual disturbances are a result of a combination of the tremendous stress the patient is being subjected to from the dynamic point of view and possible toxic effects of tetraethylthiuramdisulfide.

Urticaria of a severe nature was seen in one case (Case 21) in our series. This has been reported previously.[11] This patient had been receiving the drug for approximately five weeks when he suddenly evidenced a giant hive-like eruption associated with arthralgia, fever, and pruritus. There was no previous allergic history noted. No other drugs were being taken at the time. It should be noted that the patient was acutely disturbed for several weeks prior to the episode, and it is likely that this had some bearing on the total picture. Use of the drug was discontinued, and antihistaminics and epinephrine were given immediately, with success. Later, small amounts of the drug were again instituted, with the idea of gradually building up the dose once more. Antihistaminics were continued. There was a recurrence of the allergic manifestations. Unfortunately, the patient could not endure the difficulties he was undergoing and discontinued his association with the hospital. He then resumed drinking, but no severe reaction occurred, probably owing to the insufficient dosage of tetraethylthiuramdisulfide.

One of the most important effects associated with the administration of tetraethylthiuramdisulfide is the psychotic reaction. As more and more of the drug is being given, these reactions have become prominent. In our present series, psychotic reactions were observed in eight cases. In three of these (Cases 4, 6, and 12) they were of a relatively mild nature, occurring after hospital discharge, and were controlled with careful psychotherapy and sedation. Tetraethylthiuramdisulfide was continued safely. It is interesting to note that Cases 4 and 6 were classified originally in the neurotic group. In Case 4 some schizoid trends were exhibited. The condition in Case 12 was classified as paranoid. In the remaining five cases, 7, 9, 18, 26, and 30, rather severe reactions ensued shortly after the start of therapy. In Case 7 there was evidence of disorganization four weeks after institution of tetraethylthiuramdisulfide therapy while the patient was still in the hospital. The reaction was so alarming that discontinuance of tetraethylthiuramdisulfide and subsequent removal of the patient to a mental institution was necessary. After 24 hours, she returned to normal. The patient was felt to be a borderline schizophrenic, for whom the therapeutic relationship was too difficult and threatening to handle and who periodically required alcohol to express her instinctual drives.

One patient (Case 9) had been discharged from the hospital for three weeks and had been interviewed weekly in the outpatient department. He subsequently had an acute anxiety attack and was taken to the hospital, where physical examination disclosed no abnormalities other than marked tension and apprehension. The patient was observed to be hallucinating and revealed other evidence of disorganization. It was felt that, because of the severity of the reaction, the drug should be discontinued. Complete recovery occurred in 24 hours. Here again was a borderline schizophrenic whose tremendous need for alcohol in meeting his inner needs was threatened by tetraethylthiuramdisulfide therapy, resulting in breakdown.

Another patient (Case 18) had been discharged from the hospital for two months and had been undergoing intensive therapy in the outpatient department. Disorganization occurred and was impossible to control. Removal to the hospital with discontinuance of the drug was accomplished with prompt recovery of the patient. The patient had originally been given a diagnosis of borderline schizophrenia. The threatening effect of the drug in preventing the release of psychotic needs in alcoholic episodes is again clearly shown here.

Case 26 represents an instance in which further study prior to the institution of tetraethylthiuramdisulfide therapy might possibly have prevented what later occurred. The patient was thought to fit into the neurotic group. He was considered after the usual tests to be a satisfactory candidate and made some response to psychotherapy. The administration of tetraethylthiuramdisulfide, however, resulted in partial disorganization. The trial reactions were not wholly satisfactory, and before their completion the patient broke down, developed frank paranoid feelings, became extremely detached and affectively flattened, and exhibited incapacitating ambivalence toward help. He attempted to play one therapist against another and eventually departed precipitously from the hospital. This patient thereupon became acutely intoxicated, and a moderate tetraethylthiuramdisulfide-alchol reaction developed, which was treated in a hospital in another city. The emotional response prior to his leaving the hospital represented a schizophrenic reaction pattern, but follow-up studies regarding the outcome have been incomplete.

A patient (Case 30) who had been hospitalized for a lengthy period of time and had undergone extensive therapy expressed some resistance toward breaking up his

11. Lewis, H. M., and Bremers, H. H.: Fixed Drug Eruption from Tetraethylthiuram Disulfide (Antabuse), J. A. M. A. **142**: 1141 (April 15) 1950.

relationship with the inpatient therapist and beginning a new one in the outpatient department. Two weeks later this patient began to become disorganized and discontinued the drug voluntarily. He was subsequently readmitted to our hospital and became worse under observation, necessitating transfer to a state hospital, where he recovered rapidly. It is to be noted that removal of the drug did not affect the situation immediately as it had in other cases. Because of the existence of slight brain damage, noted previously on neurological examination and on the electroencephalogram, and because of the lack of rapid recovery on cessation of the drug, it was believed that organic factors may have complicated the picture. This complication has been noted elsewhere and tetraethylthiuramdisulfide's possible detrimental effect, through anoxia, on already damaged tissues considered.[9b] After the patient had recovered completely and was discharged, he again began drinking. He is at present hospitalized for further investigation.

ADDITIONAL RESULTS

Discontinuance of the drug in several other cases for different reasons has occurred.

Case 2.—The drug was discontinued after several weeks, while the patient was still in the hospital, because the referring agency would not undertake the responsibility for the continuation of treatment.

Case 6.—After four months of sobriety and continuous therapy, the patient suddenly discontinued the drug, became anxious and fearful, and proceeded to drink. Immediate hospitalization and resumption of therapy was successfully instituted.

Case 8.—After one month, the patient discontinued the drug voluntarily and, after a short period, became intoxicated. Thereafter, he reached sobriety and again resumed the program for two months. Since that time the clinic has not heard from him.

Case 10.—The patient continued to take the drug and maintained contact with the clinic for five months. Complete sobriety was achieved. However, she then discontinued contact but has remained sober to this date.

Case 11.—Control was well maintained with tetraethylthiuramdisulfide for approximately three months; thereupon the patient broke contact and began drinking. Later, he returned to the clinic, contrite, asking for the drug once more. At this time he is again receiving tetraethylthiuramdisulfide and being seen regularly.

Case 13.—The patient did not continue her contacts with the clinic regularly after discharge from the hospital. Five weeks of sobriety ensued, whereupon she suddenly discontinued the drug and proceeded to become intoxicated. Her contacts with the clinic were then discontinued.

Case 15.—The patient maintained clinic contact for one month subsequent to hospital discharge. No more was heard from the patient thereafter.

Case 19.—After four months of sobriety and regular outpatient attendance, the patient indicated negligence and forgetfulness in taking tetraethylthiuramdisulfide for two weeks and proceeded to become intoxicated. This episode was short-lived (one day), and he quickly resumed taking the drug under supervision. The apparent resistance to the tetraethylthiuramdisulfide program and the resistance of the patient in therapy are of interest and are seen repeatedly. Three weeks later the patient was stricken with a massive hematemesis. Prompt hospitalization with transfusion was quickly effected. Subsequent investigation failed to disclose any source for the bleeding, although the gastrointestinal tract was carefully studied. Tetraethylthiuramdisulfide was temporarily discontinued. There was a history of "nervous stomach" and frequent indigestion prior to treatment; and it is likely that a small peptic ulceration was the origin of the hemorrhage. We cannot ascribe the cause at this point to the tetraethylthiuramdisulfide therapy on an organic basis, although this matter is under investigation. It should be added, however, that at the time of the hemorrhage the patient was under intense emotional stress and was threatened by an impending change of therapists.

Case 20.—The patient maintained excellent contact and sobriety for five months and then discontinued her appointments. One month later, she called while acutely intoxicated, begging for help. She related a story of overconfidence and resentment at the necessity for taking such medication as tetraethylthiuramdisulfide. This led to discontinuance of the medication and several weeks later, a drinking episode. The patient was hospitalized again, given tetraethylthiuramdisulfide and resumed her contacts with therapy.

Case 21.—This patient has been referred to previously as the one in whom giant hives occurred. He departed from the hospital against advice and subsequently resumed drinking.

Case 24.—The patient evidenced sobriety for two months, when she suddenly discontinued the drug and became intoxicated. She was jailed for a short period and then voluntarily resumed therapy and the drug. Again, three months after the above episode, termination of her clinic contacts occurred. She indulged in a drink while taking the drug; a moderate reaction developed, necessitating hospitalization at another institution in the city. The family physician who saw her was cognizant of what had occurred and wisely referred her for care. Since that time the patient has again resumed therapy.

Case 25.—The drug was discontinued three weeks after the patient's discharge because of a diagnosis of a bleeding peptic ulcer. A suggestive history of gastritis had been present prior to the institution of tetraethylthiuramdisulfide therapy. Again no direct etiologic connection was assumed between the episode and tetraethylthiuramdisulfide.

Case 27.—The patient remained sober for two months. Thereupon he returned to the clinic for a reinforcement reaction with alcohol. Profound shock, chest pain, and cyanosis occurred. Fortunately, the patient recovered satisfactorily, but he was so disturbed by his "narrow escape" that he voluntarily discontinued his tetraethylthiuramdisulfide and clinic contacts.

Case 28.—This patient did rather well for two months and then voluntarily stopped the drug. After one week he became intoxicated. Relations with the clinic and continuance of the drug were begun once more. However, after one month the drug and clinic contacts were completely suspended.

Case 29.—The patient remained sober for five months and then voluntarily discontinued the drug. Ten days later, he began to drink. The next morning, however, fearful and anxious, he called the therapist, obviously desiring reassurance and acceptance. This was forthwith given, and he resumed therapy and the drug.

Case 31.—This patient remained sober five weeks and then discontinued the drug. One month later, the patient again resumed the program. This was followed by three separate episodes of drinking; later he resumed therapy.

Thus, of 32 patients, 10 (31%) have maintained complete sobriety to date and continue with tetraethylthiuramdisulfide therapy. One (3%) remains sober but has discontinued tetraethylthiuramdisulfide and therapy. In five (16%) psychotic reactions developed that were sufficiently severe to cause permanent discontinuance of the drug. In one case (3%) tetraethylthiuramdisulfide therapy was discontinued because of administrative reasons. Two cases (6%) involved gastrointestinal disorders which necessitated cessation of tetraethylthiuramdisulfide. Seven patients (22%) voluntarily discontinued the drug permanently. Six (19%) discontinued the drug voluntarily for a short period of time and eventually resumed therapy. Sixteen (50%) thus remain on the tetraethylthiuramdisulfide regimen and are being followed.

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IMPROMPTU REACTIONS

The danger of a tetraethylthiuramdisulfide-alcohol reaction precipitated by the patient himself must be emphasized. Two such instances have occurred in our series. The first incident (Case 26) occurred in another city. The attending physicians became cognizant of the reaction by noting the antabuse® card, which all patients carry. The second incident has already been referred to in Case 24. The purpose of these cards is similar to that with respect to the diabetic patient, who carries a card stating his medical condition. The information on the card indicates the type of drug being taken and the character of the reaction that may ensue on contact with alcohol. The name of the patient's physician is also stated.

The importance of the above precaution is obvious. It is inevitable that some patients will drink while still taking the drug, even though more efficient screening efforts, based on past experiences, may minimize this in the future. The ensuing episode may vary in intensity, depending on the total exposure, emotional implications, and the reactivity of the patient. Since the picture may simulate acute alcoholic intoxication, those confronted with the problem for the first time may not be aware of the true situation and the necessary steps to be taken. In the present series, most patients who discontinued the drug and became intoxicated did so with the apparent recognition that no reaction would result after two to three weeks' cessation of tetraethylthiuramdisulfide therapy.

Several tetraethylthiuramdisulfide-alcohol reactions have occurred under unusual circumstances. Patients have been cautioned to avoid exposure to alcohol, whether it be in the form of drink or fumes. Cough medicines, rubbing alcohol, and exotic foods containing alcoholic products have been stressed as dangerous agents. Nevertheless, one patient who had been taking tetraethylthiuramdisulfide for several months (Case 23) suddenly had a generalized convulsion, lasting several minutes. Hospitalization was immediately effected. The patient was seen one-half hour later, at which time he appeared somewhat pale and tremulous. The history revealed the following facts. The patient managed a tavern and had been working all day, when he suddenly slumped to the floor and exhibited generalized convulsive movements. There was no biting of the tongue or passage of urine. The seizure stopped spontaneously in two to three minutes. There was no previous history of such episodes. The patient had been taking no other drugs while taking tetraethylthiuramdisulfide. He had been seen regularly at the clinic and had been doing well. Examination, including a careful neurological survey, disclosed no striking features. The electrocardiogram was normal as was the electroencephalogram. Results of blood studies were also normal. Further history revealed that this patient had engaged for many hours in the cleansing of beer and alcohol glasses in a warm room in his tavern. When the lack of sufficient ventilation was brought out by questioning, the explanation became clear. The exposure to what must have been a heavy concentration of alcoholic fumes apparently resulted in an unusual reaction. This was explained to the patient and precautions advised for the future. He has since done well with no repetition of the episode.

Another patient complained of severe nausea and a feeling of warmth in the face while having an antifreeze solution placed in her car. She described the fumes as heavy, and exposure was somewhat prolonged.

One patient, meeting a friend in a restaurant, was urged to take a drink. The latter was thrust under his nose and he immediately vomited. Another patient vomited when, at a prize fight, a man nearby exhaled alcoholic fumes. It is apparent that these responses were on a purely psychogenic basis. These impromptu reactions have been noted elsewhere in the literature. It is well to emphasize to the patient what can and may occur in the absence of care.

SUMMARY

Tetraethylthiuramdisulfide is an additional adjunct in the approach to the alcoholic. Its use involves careful study and its value lies in the fact that it may institute an aversion to alcohol, since exposure of a previously sensitized person will instigate a severely disagreeable physical reaction. Thus, it can enable the patient to utilize more effectively psychotherapeutic procedures. By no means is it to be used without accompanying psychotherapeutic supervision. In cases in which the therapist has had difficulty in maintaining therapy because of the patient's constant and continuous intoxication, tetraethylthiuramdisulfide can help the patient to maintain sobriety so that he is reached. Tetraethylthiuramdisulfide can then enhance the patient's efforts to secure the necessary change in his behavior patterns, to readjust socially, to find renewed confidence, and to disrupt those paralyzing mechanisms involved in the use of alcohol.

Great care, however, should be exerted in the screening of the candidate for the drug. Study should include a careful physical and neuropsychiatric survey together with evaluation of environmental factors. From the purely physical point of view, great stress should be placed on the presence of a sound cardiovascular system, inasmuch as the outstanding fact in the tetraethylthiuramdisulfide-alcohol phenomenon is a profound vasomotor reaction. Psychiatric experience has indicated that there must be some positive reassurance that the patient is willing and able to give up his drinking as a means of gratification. Those who have demonstrated great insecurity, active resistance to help, prominent projective trends, and extreme difficulties in adjusting to people and situations are not usually good candidates for tetraethylthiuramdisulfide therapy. Further, the patient must be able to utilize help in a constructive manner, such as would be demonstrated in a therapeutic setting.

Administration of the drug initially is carried out in a hospital environment according to a definite schedule. Prior to discharge a reaction with a test dose of an alcoholic beverage of the patient's choosing is caused. The physical disturbance resulting is marked, affecting the cardiovascular, respiratory, and gastrointestinal systems. One should be prepared to deal promptly with the severe shock-like state often produced. There is some evidence that a decreased initial dosage of tetraethylthiuramdisulfide and a decreased test dose of alcohol result in less violent reactions. However, the effect of tetraethylthiuramdisulfide should serve to deter the patient from drinking, and a very mild reaction may not create a genuine fear of drinking.

At the suitable time the patient is discharged from the hospital on a maintenance dose of the drug and followed in the outpatient department. Reinforcement reactions are held periodically as indicated. Minor side-reactions to the drug over a period of time are common initially and consist of lassitude, occasional nausea, and abdominal cramps. These are usually transient. One very severe allergic reaction attributable to tetraethylthiuramdisulfide has been seen. It has been our experience that a decreased maintenance dose of tetraethylthiuramdisulfide serves to alleviate these side-reactions in many. The question as to whether a toxic factor is involved is extremely difficult to answer. We feel that the solution lies in considering the problem as the result of the combined action of alcohol removal, new stresses, toxicity of the drug, and the personality organization of the patient.

Important in the subsequent study of this group over an extended period has been the incidence of disorganization. This has been seen in eight patients, in whom three psychotic reactions were relatively mild and easily controlled. However, in the remaining five, the psychotic episodes were sufficiently severe to cause cessation of the drug. The etiology for this breakdown is felt to center about the severe threat presented by the maintenance of sobriety and, similarly, the combined and apparently inseparable threat of tetraethylthiuramdisulfide and psychotherapy. The alcoholism in many of these persons is merely a defense against a major emotional disturbance that appears when alcohol is suddenly removed and the patient loses the protective mechanisms necessary to handle increased anxiety and stress. In others the psychotic reaction appears to be a response that was used for the first time by an essentially neurotic person. We have been unable to evaluate completely the toxic factors and are continuing research in this area.

It is significant that, of 32 patients studied over a period of eight months, 16 (50%) continue tetraethylthiuramdisulfide therapy and remain in contact with the clinic. Of these, 10 (31%) have maintained complete sobriety; 6 (19%) have had intermittent relapses but have returned to the regimen.

Frequently, the patient under the strong temptation to drink may voluntarily cease taking his medication. Effective psychotherapeutic techniques will do much toward averting such action. Again, some patients may imbibe while taking the drug and unexpected reactions may occur outside of the hospital environment. It is important that one be aware of the possibility of such an occurrence in dealing with what appears to be simply alcoholic intoxication. The importance of carrying the antabuse® card at all times is stressed to patients.

51 Coventry St.

THE CAROTID SINUS

ITS CLINICAL IMPORTANCE

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It has been known for many years that pressure in the region of the carotid sinus might produce slowing of the heart, unconsciousness, and convulsions. These effects were ascribed to stimulation of the vagus nerve until the anatomic and physiological studies of Hering.[1]

Weiss and Baker [2] in 1933 called attention to the fact that a hypersensitive carotid sinus reflex was responsible for spontaneous attacks of vertigo, syncope, convulsions, and lesser symptoms. They described three types of carotid sinus syndrome: (1) the cardioinhibitory, or vagal, type with cardiac slowing or asystole, which is prevented by atropine; (2) the vasodepressor type, in which there is a decided drop in blood pressure not related to bradycardia, which may be prevented by epinephrine but not atropine; and (3) the cerebral type, in which there is loss of consciousness without significant cardiac slowing or drop in blood pressure and is not affected by atropine or epinephrine. Ferris and his coworkers [3] found 34% to be of the cardioinhibitory type, 5.3% of the vasodepressor type, and 60.7% of the cerebral type. They also described mixed forms.[4] Procainization of the carotid sinus abolished all types. Galdston and co-workers [5] studied 100 patients by continuous recording of the pulse rate and blood pressure with direct intra-arterial measurements. Twenty-six had syncope and convulsions on carotid sinus pressure, but only three had spontaneous attacks. They found that combined vagal and depressor response was the commonest, with pure vagal response next in frequency. In the author's series of 20 patients with spontaneous syncope, all showed vagal response during induced attacks. Ten were reported previously.[6] Of 10 patients whose complete mechanism was studied, 5 showed the vagal type, 4 vagal and vasodepressor types, and 1 vagal and cerebral type. In the latter, cerebral response predominated on one occasion, and vagal response predominated at other times. Of three other patients who previously showed vagal response, none showed significant response of any kind when studied during symptom-free intervals. Three more patients are reported but not included in the statistical analysis. One patient with faintness, but not syncope, is reported because he is the son of a patient

1. Hering, H. E.: Der Kerotisdruckversuch, München. med. Wchnschr. **70**: 1287, 1923; Die Karotissinusreflexe auf Herz und Gefässe, vom normal-physiologischen, pathologisch-physiologischen und klinischen Standpunkt. Gleichzeitung über die Bedeutung der Blütdruckzügler für den Normalen und abnormen Kreislauf, Dresden, Theodor Steinkopff, 1927.

2. Weiss, S., and Baker, J. P.: The Carotid Sinus Reflex in Health and Disease: Its Role in the Causation of Fainting and Convulsions, Medicine **12**: 297, 1933.

3. Ferris, E. B., Jr.; Capps, R. B., and Weiss, S.: Carotid Sinus Syncope and Its Bearing on the Mechanism of the Unconscious State and Convulsions: Study of 32 Additional Cases, Medicine **14**: 377, 1935.

4. Weiss and Baker.[2] Ferris, Capps, and Weiss.[3]

5. Galdston, M.; Goldstein, R., and Steele, J. M.: Studies of the Variation in Circulatory and Respiratory Responses to Carotid Sinus Stimulation in Man, Am. Heart J. **26**: 213, 1943.

6. (*a*) Evans, E.: The Carotid Sinus Syndrome, Geriatrics **4**: 90, 1949; (*b*) Carotid Sinus Syncope Associated with the Neurovascular Syndrome Simulating Serious Disease of Nervous System, J. A. M. A. **139**: 226 (Jan. 22) 1949.

with vagal syncope. Another patient, also the son of a patient with vagal syncope, is reported because of two spells of syncope at the time of his father's death, although he showed only carotid sinus hypersensitivity and dizziness during carotid sinus pressure when examined two months later. A third patient, with a hyperactive carotid sinus reflex, cataplexy, and narcolepsy, is the father of a patient with carotid sinus syncope plus narcolepsy and probably cataplexy.

Carotid sinus syndrome should be differentiated from the hyperactive carotid sinus reflex; the former is associated with syncope, but the latter is not.

Spells of unconsciousness may ocur abruptly, but a definite aura usually is present; dizziness, weakness, spots before the eyes, ringing in the ears, or epigastric distress may precede the attack. Hyperpnea, perspiration, and pallor usually occur, and vertigo [7] is usually prominent during attacks. Attacks usually last a few seconds to 15 or 20 minutes but average 1 to 4 minutes. The patient usually feels well between attacks; however, cases have been mentioned in which fatigue persisted for a day or more after an attack.[8] I recently observed a patient with an extremely sensitive carotid sinus, hypertension, advanced coronary disease, and congestive heart failure who stated that he thought he was going to die during chiropractic manipulation of his neck and felt exhausted for a day or so after treatment (see upper electrocardiogram in the accompanying figure).

In spite of numerous publications, the hyperactive carotid sinus is still an important and perplexing problem.

ETIOLOGY

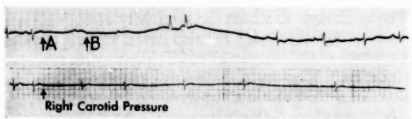
There is no satisfactory explanation why the carotid sinus becomes hyperactive in some patients, although we do know that there are several predisposing factors, including age, sex, vascular disease, especially cerebral and cardiac, medications, fatigue, emotional states, and organic diseases that increase vagal tone. It is also possible that changes in the wall of the sinus itself play a part and that there may be some familial predisposition.

In my series, the immediate family history was suggestively positive in 8 of 14 cases in which the family history of syncope was checked. The father had spells of unconsciousness in six cases; a son had spells of unconsciousness in one and faintness in another. Both sons had hyperactive carotid sinus reflexes when examined during periods when they felt well. The father of one patient with carotid sinus syncope, narcolepsy, and probably cataplexy, had hyperactive carotid sinus reflexes, narcolepsy, and cataplexy (see lower electrocardiogram in the accompanying figure). The father had spells of sleepiness and weakness, often associated with falling, precipitated by laughing or excitement. During his examination, he had a spell of weakness and collapsed without significant circulatory change. Carotid sinus pressure caused significant bradycardia and drop in blood pressure without symptoms. The family history is of further interest in this case because three of the father's uncles had spells of sleepiness, and one tended to fall and drop a violin while playing it. The latter possibly had carotid sinus syncope.

All reports emphasized age and sex. Males ranged from 85% [7] to 94%.[9] Draper,[10] in reviewing 59 cases reported in detail, found 86.5% to be in males. In my series, 80% were in males. Of the 59 cases reviewed by Draper,[10] 2 of the patients were in the third decade, 4 in the fourth, 6 in the fifth, 20 in the sixth, 21 in the seventh, and 5 in the eighth. In my series, ages ranged from 39 to 78 years, averaging 59.2 years. Hyperreactors also predominate in the upper age brackets. Seventy per cent of Nathanson's [9] 115 patients were between 50 and 70 years of age. Incidentally, 77 of his patients were without symptoms suggestive of carotid sinus syndrome. Sigler,[11] testing 1,151 males and 735 females, found that the incidence increased in adult life and reached a fastigium in middle life.

Various drugs are known to accentuate carotid sinus sensitivity, especially the vagal type.[12] These include mecholyl, morphine, digitalis, nitrites, caffeine, calcium, nicotinic acid, nicotine, strychnine, thyroid extract, eserine, salicylates, potassium cyanide, and light chloroform anesthesia. Alcohol is one of several drugs that reduces carotid sinus sensitivity.[13] One of my patients noted complete freedom from carotid sinus symptoms while under the influence of alcohol but noticed an exaggeration of the symptoms on the following day.

Heart disease predisposes to carotid sinus irritability, especially the cardioinhibitory type. Sigler [11] found that 93% of the patients with demonstrable coronary sclerosis showed significant bradycardia on carotid sinus pressure and that 55% in groups without heart disease showed significant bradycardia. According to Nathanson,[12g] 34 of his first 40 patients showing cardiac standstill following carotid sinus pressure had angina, and one-third of the patients with coronary disease and



Upper: A, right carotid sinus pressure. *B*, pressure released. Note immediate complete A-V block and sinus bradycardia followed by sinus arrest, two ectopic ventricular beats, and, finally, sinus bradycardia with partial A-V block after carotid sinus pressure of 1½ seconds. The patient was lying down and had no symptoms. *Lower:* Right carotid sinus pressure applied at *A*. Blood pressure dropped from 126/84 before carotid pressure to 102/66 one minute after the pulse rate returned to normal. It was 108/72 and 112/76 three and seven minutes later, respectively. The patient had no symptoms during the bradycardia and fall in pressure despite the erect position.

7. Smith, H. L.: A Consideration of the Hyperactive Carotid Sinus Reflex Syndrome, M. Clin. North America **31**: 841, 1947.

8. Weiss and Baker,[2] Evans,[6b]

9. Nathanson, M. H.: Hyperactive Cardioinhibitory Carotid Sinus Reflex, Arch. Int. Med. **77**: 491, 1946.

10. Draper, A. J.: The Cardioinhibitory Carotid Sinus Syndrome, Ann. Int. Med. **32**: 700, 1950.

11. Sigler, L. H.: Hyperactive Cardioinhibitory Carotid Sinus Reflex: Possible Aid in Diagnosis of Coronary Disease, Arch. Int. Med. **67**: 177, 1941.

12. *(a)* Weiss and Baker,[2] *(b)* Downs, T. M.: The Carotid Sinus as an Etiologic Factor in Sudden Anaesthetic Death, Ann. Surg. **99**: 974, 1934. *(c)* Ruzicka, E. R., and Eversole, W. H.: The Carotid Sinus in Anesthesiology: Report of 2 Cases, Lahey Clin. Bull. **3**: 47, 1942. *(d)* Sigler, L. H.: Tobacco and the Cardioinhibitory Carotid Sinus Reflex, M. Rec. **145**: 18, 1937. *(e)* Palitz, L.; Frist, T. F., and Kocour, E.: The Effects of Pressure on the Carotid Sinus at Various Altitudes: Case Reports, J. Aviation Med. **14**: 346, 1943. *(f)* Nichol, A. D., and Strauss, H.: The Effects of Digitalis, Urginin, Congestive Cardiac Failure, and Atropine on the Hyperactive Carotid Sinus, Am. Heart J. **25**: 746, 1943. *(g)* Nathanson, M. H.: Rhythmic Property of the Human Heart, Arch. Int. Med. **72**: 613, 1943.

13. Ferris, Capps, and Weiss,[3] Draper.[10]

angina were hyperreactors. Sigler [14] stated that a high degree of carotid sinus hyperactivity rarely occurred in the absence of coronary disease. In my series, 13 of 20 patients with carotid sinus syncope had obvious heart disease, 4 had myocardial infraction, 1 left bundle branch block and probably infarction, 3 angina without infarction, 3 hypertension and angina (1 with congestive heart failure), and 1 cardiac enlargement only. Another had a positive reaction to the exercise tolerance test [15] only. Two of those without definite heart disease had widespread arteriosclerosis otherwise, 3 had spontaneous episodes of temporary hemiplegia, and 1 had temporary monoplegia.

The carotid sinus reflex varies with the heart rate. Sigler [16] found the reflex to be absent in patients with marked bradycardia, greatest in patients with moderate bradycardia and greatly diminished in those with tachycardia. Increased vagal tone increased the activity of the reflex up to a certain point, beyond which it decreased.

Nathanson [9] attributed the cardioinhibitory response predominantly to vagal hypersensitivity, although he stated that it was possible that the structure of the carotid sinus in some persons was such that intrasinal pressure changes were easily transmitted to the sensory endings in the adventitia, resulting in cardiac inhibition and symptoms. The author found that the right carotid sinus was more dilated and more sensitive than the left in seven of eight patients in whom the sensitivity of both sinuses was carefully checked.[6a] He also found varying degrees of sclerosis of the sinus in 17 of 20 patients with syncope. It is of interest, however, that many patients with obvious sclerosis of the carotid sinus show no hyperactivity.

According to Sigler,[17] patients who had cerebral arteriosclerosis showed the most alarming cerebral symptoms.

Jones [18] reported a case in which inflammatory regional lymph nodes were a contributing factor.

Engel and Engel [19] found that 18 of 23 patients with acute symptoms arising in the biliary tract showed cardiac standstill of three seconds or more after carotid sinus massage. Carotid sinus hypersensitivity disappeared in 7 of 10 examined postoperatively. They interpreted these results as showing summation of afferent impulses from end organs in the biliary tract, which had reached the threshold of reaction of vagal centers in the medulla.

Several investigators emphasized emotional upsets, worry, and neurotic states in the cerebral form.[20] Evans [6a] emphasized the importance of emotional factors in the cardioinhibitory, or vagal, form. Variation in such states could readily account for some of the variability in the sensitivity of the carotid sinus. Episodes of syncope in 19 of the 20 cases in the present series were most likely to occur during periods of emotional strain or fatigue, regardless of the mechanism or combination of mechanisms. It is possible, however, that variation in the cerebral factor played a part in apparent vagal forms, because the two factors often coexist.[21] That cerebral factors played a part in many patients with vascular response was shown by Lennox and co-workers,[22] who demonstrated that even in patients with cardiovascular responses the degree of cerebral circulatory slowing was not as marked as could be produced by other procedures that did not result in loss of consciousness. Galdston and co-workers [5] found that two or more types usually occurred simultaneously, but one type predominated. They also mentioned cases in which syncope and convulsions occurred on stimulation of the side that produced the lesser degree of circulatory change and failed to occur on the side that caused the more marked circulatory response. Evans [6b] reported a case in which the cerebral form predominated on one occasion and the vagal form on other occasions.

Precipitating factors have been reported in 25% to 30% of the patients.[23] The commonest factors were sudden movements of the head, assumption of the erect position, stooping, coughing, straining at stool, shaving, tight collars, or anything causing pressure on the carotid sinus. In the present series, precipitating factors were noted in 10 of 20 cases. The notorious tight collar was a factor in three patients.

INCIDENCE

The incidence of spontaneous major seizures is unknown, but it is not uncommon, especially in males with coronary disease in the upper age brackets. Cope and associates [24] described 11 instances of spontaneous major seizures during a period in which they saw 11 patients with peptic ulcers, 4 with diabetes, 3 with active pulmonary tuberculosis, 10 with syphilis, and 1 with pernicious anemia. Weiss and Baker [2] reported 15 cases in 1933, and Ferris, Capps, and Weiss [3] observed a total of 56 through the next three years. Smith [25] reported 85 cases at the Mayo Clinic by 1937.

Overactivity of the carotid sinus without syncope is doubtless common. This is also affected by age, sex, vascular disease, and other factors. Nathanson [9] stated cardiac inhibition was as intense and as easily elicited in the asymptomatic group as it was in the group with symptoms.

DIAGNOSIS

Diagnosis is made from the history and by inducing an identical attack by pressure on one of the carotid sinuses. While the sensitivity of the carotid sinus is being tested, the patient preferrably should be in the sitting position, with the head tipped slightly backward and

14. Sigler, L. H.: The Hyperactive Cardioinhibitory Carotid-Sinus Reflex as an Aid in the Diagnosis of Coronary Disease: Its Value Compared with That of the Electrocardiogram, New England J. Med. **226**: 46, 1942.

15. Master, A. M.; Friedman, R., and Dack, S.: The Electrocardiogram After Standard Exercise as a Functional Test of the Heart, Am. Heart J. **24**: 777, 1942.

16. Sigler, L. H.: Clinical Observations on the Carotid Sinus Reflex: The Response to Carotid Sinus Pressure at Various Ages and Heart Rates and Rhythms, Am. J. M. Sc. **186**: 118, 1933.

17. Sigler, L. H.: Subjective Manifestations of the Hyperactive Carotid Sinus Reflex, Ann. Int. Med. **29**: 687, 1948.

18. Jones, M. F., and Converse, J. M.: Carotid Sinus Syndrome, Ann. Otol., Rhin. & Laryng. **50**: 806, 1941.

19. Engel, G. L., and Engel, F. L.: The Significance of the Carotid-Sinus Reflex in Biliary-Tract Disease, New England J. Med. **227**: 470, 1942.

20. (*a*) Weiss and Baker.[2] Ferris, Capps, and Weiss.[3] (*b*) Weiss, S.; Capps, R. B.; Ferris, E. B., Jr., and Munro, D.: Syncope and Convulsions Due to a Hyperactive Carotid Sinus Reflex: Diagnosis and Treatment, Arch. Int. Med. **58**: 407, 1936.

21. Weiss and Baker.[2] Ferris, Capps, and Weiss.[3] Galdston, Goldstein, and Steele.[5]

22. Lennox, W. G.; Gibbs, F. A., and Gibbs, E. L.: Relationship of Unconsciousness to Cerebral Blood Flow and to Anoxemia, Arch. Neurol. & Psychiat. **34**: 1001, 1935.

23. (*a*) Smith, H. L., and Moersch, F. P.: Further Study on the Hypersensitive Carotid Sinus Reflex Syndrome: Report of 31 Additional Cases, Proc. Staff Meet., Mayo Clin. **11**: 380, 1936. (*b*) Draper.[10]

24. Cope, R. L.; Engelhardt, H. T., and Baird, V. C.: The Carotid Sinus Syndrome: Its Importance in Clinical Medicine, Texas State J. Med. **44**: 30, 1948.

25. Smith, H. L.: Fainting Attacks Resulting from Hypersensitive Carotid Sinus Reflexes, Am. Heart J. **14**: 614, 1937.

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turned away from the side being examined. The sinus usually is situated below the angle of the jaw at the upper border of the thyroid cartilage. Sometimes the carotid bulb is readily palpable. Pressure is gradually made with the thumb so that the sinus is compressed against the spinal column.[26] Sudden pressure is undesirable, and massage should be avoided.[a] Unduly prolonged pressure may be fatal.[27] As a rule, characteristic response will occur in 10 to 25 seconds. Bilateral stimulation is dangerous,[26b] and repeated stimulation should not be done after diagnosis is made, because of occasional serious complications.[28] Askey described seven cases of hemiplegia that occurred immediately after carotid sinus pressure.[28e]

Carotid sinus syncope should be considered in the differential diagnosis when dizziness, faintness, and unconsciousness, with or without convulsions, are present. Other conditions that frequently must be differentiated are idiopathic epilepsy (petit and grand mal); narcolepsy; cataplexy; postural hypotension; hypoglycemia; several cardiac disturbances associated with asystole, tachycardia of various sorts, and aortic stenosis; and vasovagal syncope. The latter is the commonest cause of syncope, and its relation to sudden emotional stimuli, such as the sight of blood, fright, and pain, is usually clear. The onset of the attack is associated with sweating. In postural hypotension, the drop in blood pressure and transient unconsciousness are associated with assumption of the upright position. Although carotid sinus syncope may be precipitated by pain or assumption of the upright position, it may be differentiated from the previous conditions by being reproducible on carotid sinus pressure. Spontaneous hypoglycemia usually occurs two to four hours after meals and is associated with a low blood sugar level. Weiss and Baker [2] and Freedberg and Sloan [29] were unable to find any relation of the carotid sinus to idiopathic epileptic seizures. Robinson [30] examined 1,000 institutional patients with epilepsy, all of whom had been admitted because of syncope, convulsions, or transient loss of consciousness, and found that nine (0.9%) had a hyperactive carotid sinus reflex.

Differentiation in patients with heart disease is not always easy. Various degrees of heart block sometimes persist in patients with Adams-Stokes attacks. Auricular and ventricular tachycardia and auricular fibrillation or flutter may be noted during attacks in patients whose unconscious spells are associated with these disorders. Cookson [31] found 15 syncopal or epileptiform attacks in 200 patients with acute myocardial infarction. I found extremely sensitive carotid sinuses in two patients who had spells of unconsciousness during several attacks of myocardial infarction. Levine [25d] stated that syncope and angina were peculiarities of aortic stenosis. He thought that syncope could be linked up with peculiarities of the carotid sinus reflex but stated that, in most cases of aortic stenosis, normal sensitivity of the carotid sinus was found. Syncope in aortic stenosis usually occurs on exertion. An unusual clinical syndrome, consisting of glossopharyngeal tic douloureux and cardiac arrest, has been reported.[32] It consists of pain in the pharynx and at the base of the tongue, cardiac slowing or arrest, fall in blood pressure, and occasionally syncope.

Occasionally other diseases, especially Ménière's disease, may complicate the picture.[25a] Craig and Smith [33] described a case in which division of the upper portion of the eighth nerve relieved syncopal attacks after carotid sinus denervation failed. In one of my patients, pronounced vertigo was relieved elsewhere by intracranial division of the vestibular division of the eighth nerve, but syncope and convulsions were not relieved until both carotid sinuses were denervated.[25a] The neurovascular syndrome [34] complicated the diagnosis in one case previously reported.[19] This is a syndrome in which paresthesias, numbness, and pain in the fingers and hand appear in certain persons when the arm is hyperabducted. Narcolepsy and probably cataplexy were associated with carotid sinus syncope in another case. The patient, a 39-year-old man, had spells of sleepiness, weakness precipitated by laughing, and unconsciousness. Unconsciousness could be produced by carotid sinus pressure, which caused bradycardia and a fall in blood pressure.

To avoid error in diagnosis, it is important to remember that many persons who exhibit symptoms on carotid sinus pressure do not have spontaneous attacks. Even unconsciousness and convulsions occur in some patients who never have spontaneous attacks. It is also well to remember that some patients who complain of dizziness, faintness, or unconsciousness without evidence of disease of the central nervous system do not have them on the basis of carotid sinus sensitivity.

PROGNOSIS

Prognosis for patients with the carotid sinus syndrome per se is good. Many patients with mild symptoms are not affected seriously, but those with serious symptoms may be greatly handicapped. It is possible that in rare instances marked spontaneous carotid sinus overactivity may be the cause of cerebral vascular accidents. Temporary hemiplegia in three of my patients possibly could

26. Askey, J. M.: Technique of Carotid Sinus Stimulation, California & West. Med. **63**: 266, 1945.

27. Marmor, J., and Sapirstein, M. R.: Bilateral Thrombosis of Anterior Cerebral Artery Following Stimulation of a Hyperactive Carotid Sinus, J. A. M. A. **117**: 1089 (Sept. 27) 1941.

28. (*a*) Weiss, Capps, Ferris, and Munro.[26b] Marmor and Sapirstein.[27] (*b*) Gibbs, F. A., and Forster, F. M.: Electroencephalographic Studies on Carotid Sinus Syncope, Tr. Am. Neurol. A. **67**: 143, 1941. (*c*) Engel, G. L.; Romano, J., and McLin, T. R.: Vasodepressor and Carotid Sinus Syncope; Clinical Electroencephalographic and Electrocardiographic Observations, Arch. Int. Med. **74**: 100, 1944. (*d*) Levine, S. A.: Clinical Heart Disease, ed. 3, Philadelphia, W. B. Saunders Company, 1945, p. 317. (*e*) Askey, J. M.: Hemiplegia Following Carotid Sinus Stimulation, Am. Heart J. **31**: 131, 1946. (*f*) Zeman, F. D., and Siegal, S.: Monoplegia Following Carotid Sinus Pressure in the Aged, Am. J. M. Sc. **213**: 603, 1947. (*g*) Brannon, E. S.: Hemiplegia Following Carotid Sinus Stimulation; Case Report, Am. Heart J. **36**: 299, 1948.

29. Freedberg, A. S., and Sloan, L. H.: Association of Carotid Sinus Reflexes with Syncope and Convulsions: Report of 4 Cases, Arch. Neurol. & Psychiat. **38**: 761, 1937.

30. Robinson, L. J.: Syncope, Convulsions and Unconsious State: Relation to Hyperactive Carotid Sinus Reflex, Arch. Neurol. & Psychiat. **41**: 290, 1939.

31. Cookson, H.: Fainting and Fits in Cardiac Infarction, Brit. Heart J. **4**: 163, 1942.

32. Riley, H. A., and others: Glossopharyngeal Neuralgia Initiating or Associated with Cardiac Arrest, Tr. Am. Neurol. A. **68**: 28, 1942. Browder, E. J.: Unpublished data. Ray, B. S., and Stewart, H. J.: Glossopharyngeal Neuralgia: Cause of Cardiac Arrest, Am. Heart J. **35**: 458, 1948.

33. Craig, W. M., and Smith, H. L.: The Surgical Treatment of Hypersensitive Carotid Sinus Reflexes: Report of 13 Cases, Yale J. Biol. & Med. **11**: 415, 1939.

34. Wright, I. S.: The Neurovascular Syndrome Produced by Hyperabduction of the Arms: Immediate Changes Produced in 150 Normal Controls, and Effects on Some Persons of Prolonged Hyperabduction of Arms as in Sleeping, and in Certain Occupations, Am. Heart J. **29**: 1, 1945.

have been on this basis. In any event, one can readily realize the danger in certain occupations and driving cars. Two patients in the present series had minor automobile accidents during syncope, and another fell and fractured her arm.

In general, prognosis depends on associated diseases, especially coronary and cerebral arteriosclerosis and hypertension, so that accurate prognosis requires the evaluation of these diseases.

TREATMENT

If the symptoms are mild and the attacks infrequent, no treatment other than explanation of the attack and reassurance are necessary. Fatigue, worry, and emotional upsets should be avoided if possible. Patients should be instructed to avoid factors that precipitate attacks, especially turning the head quickly, looking up, arising or stooping suddenly, and wearing tight collars. Sedatives are helpful. Banthine* (beta-diethylaminoethyl xanthene-9-carboxylate), 50 to 100 mg., three or four times daily, controlled symptoms in six of my patients, although the carotid sinus reflex was still somewhat hyperactive on carotid sinus pressure in four. A fifth patient, a 46-year-old man, who had predominately the vagal type of syncope during three periods of carotid sinus irritability in 11 years, took banthine* for two months. Two months after he stopped medication, the carotid sinus was not found to be sensitive. Longino and co-workers [35] were able to block the vasopressor effect of bilateral carotid sinus pressure with this drug. Other drugs that have been particularly useful are atropine in the vagal type and ephedrine in the vasodepressor type.

Surgery [36] is sometimes necessary in severe conditions not responding to medical management. Preliminary procaine injection should be made to test response. Craig and Smith [23] denervated the sinus in 12 cases and had excellent results in 4, good in 1, fairly good in 4, and poor results or failures in 3. Turner and Learmonth [37] reported a case in which bilateral denervation cured the patient without ill effects. Severe vertigo was alleviated by intracranial section of the vestibular portion of the eighth nerve of one of my patients, but bilateral denervation of the carotid sinus was necessary to relieve syncope and convulsions. Now, two years after his operation, he still has carotid sinus hypersensitivity, so that he cannot wear a tight collar, get up quickly, or turn his head suddenly. Previously, sinus pressure immediately caused asystole, syncope, and convulsions. Now, slight pressure causes dizziness and ectopic ventricular beats without significant blood pressure changes. Ray and Stewart [38] found that intracranial division of the glossopharyngeal nerve permanently abolished the effects of pressure on the homolateral sinus. They considered this procedure valuable when a condition of local tissues might make local surgery undesirable or impossible. In some cases, removal of local pathology is curative.[18] Stevenson and Moreton [39] treated 24 patients with roentgen therapy. In 16 the condition was of the vagal and in eight of the cerebral type. Complete relief was obtained in 44% and partial relief in 25%.

SUMMARY AND CONCLUSIONS

1. The clinical importance of the hyperactive carotid sinus reflex and carotid sinus syncope is discussed.

2. Twenty cases of carotid sinus syndrome, one possible carotid sinus syndrome, and two interesting cases of the hyperactive carotid sinus reflex are discussed.

3. The carotid sinus syndrome is an important disease that is commonly overlooked and is doubtless more frequent than generally realized.

4. It is predominantly a disease of men in the upper age brackets but should be suspected in all patients with dizziness, faintness, syncope, or convulsions.

5. Emotional states, such as anxiety or worry, and fatigue are usually associated with exacerbation of symptoms in the vagal as well as in the cerebral and mixed forms of carotid sinus syncope.

6. The carotid sinus may not be found to be hyperactive on pressure during periods when the patient is without symptoms.

7. Family histories suggest a familial tendency.

8. Other diseases, particularly coronary or cerebrovascular disease, are usually present, and prognosis mainly depends on these diseases.

9. Complicating diseases, such as the neurovascular syndrome, Ménière's disease, narcolepsy, and cataplexy in this series, may make the diagnosis appear more difficult or the prognosis appear more serious.

10. Most patients respond well to medical management, but occasionally surgery is necessary. Banthine* (beta-diethylaminoethyl xanthene-9-carboxylate) appeared to be clinically effective in six cases in which it was used.

601 Magnolia St.

35. Longino, F. H.; Grimson, K. S.; Chittum, J. R., and Metcalf, B. H.: An Orally Effective Quarternary Amine, Banthine, Capable of Reducing Gastric Motility and Secretions, Gastroenterology **14**: 301, 1950.

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Estimate of Future Number of Veterans.—The United States Government is building for use by the Veterans Administration 78 new hospitals to add to the 136 now in operation. This multimillion dollar venture, which will bring the total bed capacity of Veterans Administration Hospitals up to 143,000, is only a fraction of a tremendous building program which will allegedly be required to care for the estimated 300,000 veterans who will be sick by 1975. Such estimates, furthermore, are only on the basis of our current veterans population of 19,000,000 souls. Stable, indeed, would be the imagination which did not reel at the prospect of the further expansion which, if this policy is continued, will follow the Korean War and universal military service. Under present methods of interpreting eligibility laws the number of eligibles for care will eventually not fall far short of a figure which will include all the adult males, and many of the females, in the country, and so reach an order of magnitude of over 60,000,000.—Richard Warren, M.D., Are Veterans People? *Connecticut State Medical Journal*, March, 1952.

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EFFECTS OF BARBITURATE SEDATION ON THE BRAIN IN TOXEMIA OF PREGNANCY

Milton L. McCall, M.D.
and
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Recently quantitative studies of cerebral circulation and metabolism have been carried out on women with toxemia of pregnancy.[1] It was found that the cerebral blood flow was not affected by any type of toxemia. The most striking departure from normal was the presence of a greatly increased cerebrovascular resistance, thought to be due to vasospasm. In eclampsia with convulsions, there was a depression of cerebral oxygen metabolism. This knowledge has given us a new insight into the pathophysiology of the brain in toxemia of pregnancy and has opened the way to the evaluation of the effects of therapy on this organ.[2]

In modern times one of the most important aspects of therapy in this disease of obscure causation has been the use of large amounts of sedatives in an attempt to prevent or allay convulsions by depressing the central nervous system. The mechanism of this cerebral depression has not been clearly understood, and it would appear to be of the utmost importance to evaluate the drugs that affect the nervous system in this way, especially since toxemia itself may bring about a depression of cerebral oxygen metabolism.

At present the barbiturates are probably used as frequently in toxemia as are any other group of sedatives. Since Fischer and Von Mering [3] first demonstrated the hypnotic effect of barbituric acid, in 1903, many barbiturate derivatives have been used in toxemia. This report deals with the effects of three of the most popular members of the group, amobarbital (amytal®) sodium, thiopental sodium, and phenobarbital (luminal®) sodium.

METHODS AND MATERIAL

The method of Kety and Schmidt [4] was used. This involves the simultaneous withdrawal of venous blood from the jugular bulb and arterial blood from the femoral artery over a period of 10 minutes while the patient is breathing a mixture of 15% nitrous oxide, 21% oxygen, and 64% nitrogen. Mean arterial blood pressure is measured directly from the femoral artery with a damped mercury manometer. Blood gas analyses of nitrous oxide, oxygen, and carbon dioxide were made with the Van Slyke-Neill apparatus. As previously described,[1] cerebral blood flow (CBF) was measured in cubic centimeters per 100 gm. of brain per minute. Cerebral oxygen metabolism ($CMRo_2$) was calculated in cubic centimeters of oxygen utilized per 100 gm. of brain per minute, and cerebrovascular resistance (CVR) in millimeters of mercury pressure per cubic centimeter of blood flow per 100 gm. of brain per minute. The respiratory quotient (RQ) was calculated by computing the relationship between the oxygen uptake by the brain and the amount of carbon dioxide given off $\frac{(V-A\ co_2)}{(A-V\ o_2)}$.

Thirty-two women in the latter weeks of pregnancy were studied; 15 had preeclampsia per se, and 17 had acute toxemia superimposed on mild essential hypertension. It had been shown in our earlier work that there is no significant difference between these two types of nonconvulsive toxemia as far as cerebral function is concerned. No therapy was given for at least 12 hours before the control experiment (C). Immediately after the first flow the sedative being studied was administered, and the second observation (E) was carried out as soon as the drug had taken effect.

RESULTS

Amobarbital Sodium.—Amobarbital (isoamylethyl barbituric acid) was first described by Shonle and Moment,[5] in 1923. In 1926 Page and Coryllos [6] prepared the sodium salt and used it to anesthetize animals experimentally. Zerfas and his co-workers [7] in 1929 reported on the induction of anesthesia in man by its intravenous use. Since that time amobarbital sodium has been used extensively in toxemia of pregnancy.[8]

Eleven patients were given amobarbital sodium in 10% solution intravenously until unconsciousness took place. The dosage varied from 3¾ to 7½ grains (0.23 to 0.50 gm.). Deep anesthesia was avoided in every case,

TABLE 1.—*Mean Effects of Use of Amobarbital Sodium on Cerebral Function**

MABP Mm. Hg		A—Vo_2 Vol. %		CBF Cc./100 Gm. Brain/Min.		$CMRo_2$ Cc./100 Gm. Brain/Min.		CVR Mm. Hg Cc./100 Gm. Brain/Min.		RQ	
C	E	C	E	C	E	C	E	C	E	C	E
125	113†	6.5	5.6‡	59	48§	3.8	2.7†	2.3	2.4	0.90	1.10

* MABP, mean arterial blood pressure; A—Vo_2, arteriovenous oxygen difference; CBF, cerebral blood flow; $CMRo_2$, cerebral oxygen metabolic rate; CVR, cerebrovascular resistance; RQ, respiratory quotient; C, control flow; E, after medication.
† Statistically significant change ($p < 0.01$).
‡ Statistically significant change ($p < 0.05$).
§ Statistically significant change ($p < 0.02$).

and, in the majority of instances, the patients were restless and reacting by the end of the 10-minute period of the experiment.

As seen in table 1, the mean arterial blood pressure (MABP) was significantly lowered from a mean of 125

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Read before the Section on Obstetrics and Gynecology at the One-Hundredth Annual Session of the American Medical Association, Atlantic City, June 13, 1951.

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to 113 mm. Hg. The arteriovenous oxygen difference ($A—Vo_2$ was significantly depressed from 6.5 to 5.6 vol. %. The cerebral blood flow was reduced from 59 to 48 cc. per 100 gm. of brain per minute, and there was a highly significant lowering of oxygen utilization by the brain ($CMRo_2$) from the pretreatment level of 3.8 to 2.7 cc. per 100 gm. of brain per minute following the administration of amobarbital sodium. The cerebrovascular resistance (CVR) was essentially unchanged by this type of sedation, being 2.3 before and 2.4 mm. Hg per cubic centimeter per 100 gm. of brain per minute immediately thereafter. The respiratory quotient (RQ) remained within normal limits.

Thiopental Sodium.—Thiopental sodium, a short-acting thiobarbiturate, was introduced clinically in 1935 by Lundy.[9] Recently its use in toxemia of pregnancy has been fostered by Aubanel.[10] Short,[11] and Browne.[12]

Nine toxemic pregnant women were given this drug intravenously in a 2.5% solution until consciousness was barely lost. Total dosage varied from 0.2 to 0.9 gm. All patients reacted either during or shortly after the 10-minute experimental period that immediately followed the injection.

TABLE 2.—*Mean Effects of Use of Thiopental Sodium on Cerebral Function**

MABP Mm. Hg		A—Vo_2 Vol. %		CBF Cc./ 100 Gm. Brain Min.		$CMRo_2$ Cc./ 100 Gm. Brain Min.		CVR Mm. Hg Cc./100 Gm. Brain Min.		RQ	
C	E	C	E	C	E	C	E	C	E	C	E
115	110	6.3	6.0	55	46†	3.4	2.7‡	2.1	2.4	1.0	1.0

* See footnote *, table 1.
† Statistically significant change ($p < 0.02$).
‡ Statistically significant change ($p < 0.001$).

As seen in table 2 the mean arterial blood pressure was lowered from 115 to 110 mm. Hg. The uptake of oxygen by the brain ($A—Vo_2$) was little affected, being 6.3 vol. % before and 6.0 vol. % after administration of the drug. Cerebral blood flow was significantly reduced from a mean of 55 cc. to 46 cc. per 100 gm. of brain per minute. There was a decided depression of the oxygen utilization by the brain from 3.4 cc to 2.7 cc. per 100 gm. of brain per minute. Cerebrovascular resistance was slightly increased after administration of thiopental sodium to 2.4 mm. from 2.1 mm. Hg per cubic centimeter per 100 gm. of brain per minute. The respiratory quotient was exactly unity before and after sedation.

Phenobarbital Sodium.—Phenylethyl barbituric acid (phenobarbital, [luminal®]) was patented in 1912. According to Lundy and Osterberg,[13] Hauptmann [14] in the same year was one of the first to report its use. It is a long-acting barbiturate reputed to be especially efficacious as an anticonvulsant in epilepsy.[15] Phenobarbital

TABLE 3.—*Mean Effects of Use of Phenobarbital Sodium on Cerebral Function**

MABP Mm. Hg		A—Vo_2 Vol. %		CBF Cc./ 100 Gm. Brain Min.		$CMRo_2$ Cc./ 100 Gm. Brain Min.		CVR Mm. Hg Cc./100 Gm. Brain Min.		RQ	
C	E	C	E	C	E	C	E	C	E	C	E
123	120	6.3	6.6	53	48	3.4	3.2	2.4	2.5	0.95	0.98

* See footnote *, table 1.

and its sodium salt have long been used in toxemia of pregnancy.

Twelve patients were given 7½ grains (0.50 gm.) of phenobarbital sodium intramuscularly after the completion of the control experiment. The second investigation was carried out an average of one hour after administration of the sedative. A surprising clinical feature was the fact that none of these patients showed more than slight drowsiness at the time of the second experiment. There were no significant deviations from normal cerebral function. The mean arterial blood pressure decreased from 123 mm. to 120 mm. Hg. Cerebral blood flow was lessened only 5 cc. per 100 gm. of brain per minute. The cerebral metabolic rate, in terms of oxygen, and the cerebrovascular resistance remained approximately the same as did the respiratory quotient.

BLOOD GASES

The oxygen content of the arterial blood was lowered from 14.6 to 13.9 vol. % by administration of amobarbital sodium and from 14.0 to 13.3 vol. % by administration of thiopental sodium. This must be regarded as due to slight desaturation of the blood with oxygen, inas-

TABLE 4.—*Mean Effects of Barbiturate Sedation on Blood Gases*

		Arterial				Internal Jugular			
		O_2 Content		CO_2 Content		O_2 Content		CO_2 Content	
		Vol. %				Vol. %			
No. of Patients	Drug	C*	E†	C	E	C	E	C	E
11	Amobarbital sodium	14.6	13.9‡	41.9	41.5	8.3	8.9	47.5	47.4
9	Thiopental sodium	14.0	13.3	40.0	39.5	7.6	7.3	45.6	45.6
12	Phenobarbital sodium	14.2	14.1	39.1	36.9	7.8	7.6	42.1	42.2

* Control flow.
† After medication.
‡ Statistically significant change ($p < 0.05$).

much as there is no change in hemoglobin content or oxygen capacity in the few minutes between experiments. Mild respiratory depression by these intravenously administered sedatives with resultant minimal anoxic anoxia undoubtedly is the fundamental cause. There is no such depression of arterial oxygen following administration of phenobarbital sodium when the patient is still

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awake and obviously affected to a lesser degree. The arterial carbon dioxide and the venous oxygen and carbon dioxide were not significantly affected by administration of any of the barbiturates.

COMMENT

This study shows that amobarbital sodium and thiopental sodium, intravenously administered in minimal doses to cause unconsciousness, bring about marked change in cerebral function in toxemic pregnant women. On the other hand, phenobarbital sodium administered intramuscularly in large dosage caused neither clinical effect nor significant change in cerebral function.

The cerebral oxygen metabolism was the function most affected. There was a 29% depression after administration of amobarbital sodium and a 21% depression after administration of thiopental sodium. It has been shown by Himwich and her co-workers [16] that full anesthetic doses of thiopental sodium in normal man lowers this function 36%. Wechsler, Dripps, and Kety [17]

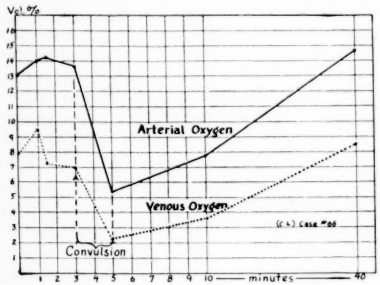

Fig. 1.—Depression of arterial and venous oxygen in comatose state.

have further brought out that there is an increasing depression of cerebral oxygen metabolism as larger doses of the drug are given.

The mechanism of this depression is not entirely clear. The fact that it takes place in the presence of a basically undiminished oxygen supply in the arterial blood being brought to the brain seems to validate the assumption that the brain cells themselves are unable to utilize oxygen as well. This resembles histotoxic anoxia and may be brought about by paralysis of some portion of the neuraxon, thus slowing down its activity, or an interference with the normal functioning of the enzyme systems.[18] As shown in our previous work, the same situation exists in the coma of eclampsia. In fact this is true in all types of coma thus far studied,[19] and there seems to be a correlation between the degree of mental clearness present and the level of the cerebral metabolic rate. There is one notable exception to this, for it has recently been shown [20] that in the physiological unconsciousness of normal sleep the oxygen metabolism of the brain remains normal. This at once brands the depressions brought about by coma and anesthesia as pathological.

Aside from the histotoxic anoxia present during the comatose stage of eclampsia, there is also anoxic anoxia due to respiratory difficulties during the convulsion. Although cyanosis and clinical evidence of anoxemia during this state is familiar, the full significance of the extent of this anoxia was not apparent until an eclamptic convulsion was experienced in the midst of a blood flow experiment.[21] Blood gas determinations were done immediately before, during, and after the episode. This, so far as we

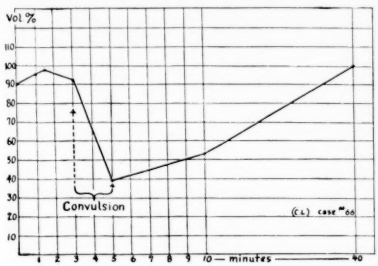

Fig. 2.—Saturation of hemoglobin with oxygen.

know, is the first case in which such observations have been made. During the first 10 minutes the patient breathed 85% oxygen and during the subsequent 40 minutes 100% oxygen.

Figure 1 shows the depression of arterial oxygen from a level of 13.6 vol. %, 10 seconds before the convulsion started, to 5.8 vol. % toward the end of the convulsion. The venous concentration of oxygen shows a comparable depression. Figure 2 shows the great drop in oxygen saturation of the blood to a level of 39% during the convulsion and the gradual rise to normal after 40 minutes

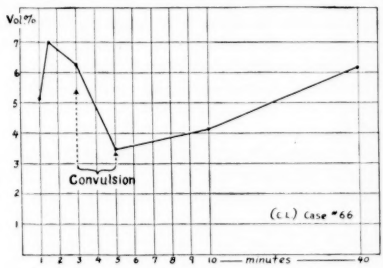

Fig. 3.—Uptake of oxygen by the brain.

with inhalation of 100% oxygen. In figure 3 the uptake of oxygen by the brain ($A—Vo_2$) is shown to be decreased almost 50%, from 6.6 to 3.5 vol. %.

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It is therefore evident that eclampsia is a disease associated with oxygen deprivation and deficient uptake of oxygen by the brain during the convulsive stage and a compromised cellular oxygen metabolism in the presence of normal oxygen supply during the comatose phase. At present there is no method capable of measuring cerebral blood flow in man at the very moment of convulsion. This has been done in animals,[22] and a great increase in oxygen metabolism and blood flow followed by reduced cerebral oxygen metabolism in the immediate postconvulsive phase, similar to that in man, has been shown.

From the practical point of view the question is immediately posed as to whether this type of sedation is harmful or efficacious when used in toxemia. If, in preeclampsia, convulsions with their deleterious effect on the brain can be prevented with moderate doses of sedation and relatively harmless transient depression, it would appear to be most desirable. If eclampsia occurs in spite of such therapy, however, the histoanoxic effect of the disease is superimposed on that of the drug. In eclampsia, although it is important to prevent repeated convulsions with their exhaustive effect on the brain, it also seems logical that the use of large and continued doses of drugs adding to the depression of the postconvulsive comatose state would be contraindicated from the standpoint of possible permanent cerebral damage. Selle [23] showed that certain barbiturates reduce survival time and activity of the primitive respiratory mechanism of isolated head preparations, which bears out this contention. Clinically we have repeatedly gained the impression that overtreatment with sedation not only prolongs the coma of eclampsia but also adds to the morbidity and mortality. We have found intravenously administered barbiturates to be particularly pernicious in this connection and have been especially perturbed by the restlessness and inevitable associated fatigue so often seen, which may be a manifestation of the histoanoxic state present within the brain.

The increase of cerebrovascular resistance, which is the most significant abnormality found in all types of toxemia of pregnancy, was not favorably affected by barbiturate sedation. In fact, there was a slight rise in the degree of vasospasm within the brain after the use of these drugs. It has been previously pointed out that barbiturates have a mild hypotensive effect [24] in man. This was also shown to be true in preeclampsia. This effect is reputed to be due to a combination of central effect and a local dilating action directly on the vascular musculature.[25] Our study reveals that the brain does not join in this effect, and the inference is that the vasodilatation is brought about in other portions of the body. What possible role cerebral vasoconstriction may play in bringing about abnormal electrical patterns in the brain and convulsions is unknown.

Cerebral blood flow, which is normal in both convulsive and nonconvulsive toxemias of pregnancy, was significantly depressed. This was due to the lowering of systemic blood pressure and a slight increase in cerebrovascular tone.

The intravenously administered barbiturates obviously do not correct the pathophysiological condition of the brain present in toxemia of pregnancy. In fact, it is likely that they may cause further deterioration. Because at the present time sedation remains an important aspect of therapy in toxemia, it is important that all sedatives commonly used in this disease be carefully studied in order that one may ascertain which are the least harmful.

SUMMARY

Quantitative studies of cerebral blood flow, cerebral oxygen metabolism, cerebrovascular resistance, arteriovenous oxygen difference, mean arterial blood pressure, respiratory quotient of the brain, and the blood gases were made in 32 toxemic pregnant women before and after administration of amobarbital (amytal®) sodium, thiopental sodium, or phenobarbital sodium. Phenobarbital sodium, given in 7½ grain (0.50 gm.) doses intramuscularly, produced but minimal clinical effect and did not alter any of the cerebral functions studied. Amobarbital sodium and thiopental sodium given intravenously, so as to bring about light anesthesia, produced the following effects: (*a*) highly significant depression of the oxygen utilization by the brain, (*b*) significant lowering of cerebral blood flow, and (*c*) mild depression of mean arterial blood pressure. The elevated cerebrovascular tone that is present in typical cases of toxemia of pregnancy, was not relieved by administration of any of the barbiturates studied.

1930 Chestnut St. (Dr. McCall).

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Acute Otitis Media.—Acute infections of the middle ear continue to be a serious problem in the everyday practice of medicine. Although the widespread use of the various potent antimicrobial agents has greatly modified these inflammatory processes, the incidence of complicating chronic otitis media and middle ear fibrosis has not been decreased correspondingly. It seems probable that, when statistics become available, they will show not only a relative increase in the chronic suppurative processes, but more important, an increase in the resultant progressive deafness. . . . Antimicrobial therapy, which produces a rapid drop in fever and relief of pain together with the marked decrease in immediate serious complications, has resulted in the physician's being lulled into a false sense of security. This complete faith in antimicrobial therapy has led to the neglect of other useful therapeutic measures and has also produced a tendency to carry poorly responding cases into a danger period. Valuable time is lost either by shifting to other antibiotics or by increasing doses, when a well performed myringotomy or simple mastoidectomy would have resulted in prompt clearing of the infection with preservation of hearing.—Thomas Timothy Smith, Acute Otitis Media, *Postgraduate Medicine*, March, 1952.

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TOWARD A REGIONAL PROGRAM IN MEDICAL EDUCATION

William J. McGlothlin, Atlanta, Ga.

If someone had predicted in 1947 that five years later the southern states would be transferring over a million dollars across state lines to help support professional schools in medicine, dentistry, veterinary medicine, and social work, he would have been called visionary or, more likely, idiotic, for there was no precedent for transfer of educational funds to anything like that extent. To be sure, West Virginia and Virginia had executed a contract in 1946 under which the Medical College of Virginia agreed to accept 20 third-year medical students upon payment of $1,000 per student per year. That program, though a beginning, was necessarily small. It could hardly foreshadow the organization of the Southern Regional Education Board, under a 14-state compact, which now guides a program affecting 850 students, 19 public and private universities, and 14 states. The board itself brings together educational and political leaders to help institutions plan programs of benefit to the region in ways that transcend state lines.

Why and how did such a startling program develop? Obviously, without fairly strong motivation, a legislature would hardly agree to help support institutions located outside the borders of its state. The legislatures must have felt a strong and compelling need for a program of this sort, for they did so agree. How did that come about? Southern governors had begun talking about the possibility of such a program in 1939-1940, when the Southern Governors' Conference began a series of annual meetings. The governors were impressed by the ever-increasing costs of education. No end to that increase seemed possible; nevertheless, the governors recognized that more, rather than less, education was needed. They saw that the serious problems that grew out of the South's inadequate development of graduate and professional schools in many fields were causing the South to lose its educational investment in many of its most capable young persons. Too often highly competent students had to leave the region to obtain specialized training from graduate and professional schools located in more favored parts of the country. They naturally made professional contacts in the vicinity of the schools they attended and often settled there, contributing their productive years to the newer environment. This kind of loss was sufficiently large to cause alarm, but it was perhaps even more serious that large numbers of capable youngsters never got to graduate or professional schools at all because they were not easily accessible. The area from which any school draws its students is sharply limited. Findings of a 1936 study of student migration make it clear that even so noted an institution as the University of Chicago draws the preponderant majority of its students from within a 250 mile radius.

The problem was, therefore, sharply posed. On the one hand, expansion of graduate and professional schools was necessary to the constant improvement of living in the South. Physicians, engineers, lawyers, social workers, chemists, physicists, and a host of other specialized persons at high levels of training were needed to continue the advances that the South was beginning to make with increasing speed. To supply them, additional funds for education were clearly needed. On the other hand, the economic level of the region was inadequate to support fully developed programs of graduate and professional education in every state, even if that were desirable.

As the governors continued these discussions up to 1945, one possible aid toward the solution of the problem became clear. Some needs could be met by regional action. The states could join forces so that no state would feel required to provide within its borders all kinds of educational programs in order to meet the needs of its students. One or more medical schools might eventually be needed in every state because of the health needs and student demands in that field, but it was clearly not necessary in certain other schools, such as forestry, where six schools could easily serve the requirements of the region. What the governors hoped to find were ways in which joint planning could satisfy regional needs with a minimum of waste. The objective would be to locate, somewhere in the region, facilities in accordance with the need—no more, no less. If this end could be achieved, the South's students would find close at hand opportunities for development of their innate capacities. The loss of capable youngsters could be reduced, and the balance sheet of trained leadership available to the region could begin to be written in black rather than in red.

These were not new ideas to educational thought. Educators had been talking about regional planning in education for a number of years. In the early thirties many had proposed regional planning as one means of more effective expenditure of funds in higher education. They believed that the size of the area a school can serve effectively is in inverse relation to the extent of demand and need for the opportunities that school provides; for example, universal free education means that virtually every child reaching the age of 6 attends an elementary school of some sort. The demand and need is, therefore, high, and the numbers of students involved are great. As a result, each school can serve only a small area. On the other hand, highly specialized work in Egyptology might be needed at only one graduate school in the United States in order to satisfy national demand and need. In between are demands and needs that can be most efficiently met by counties, states, or regions. If this theory is valid, and educational experience seems to support it, it has a corollary that a school should be able to

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Read before the Forty-Eighth Annual Congress on Medical Education and Licensure, Chicago, Feb. 11, 1952.

draw support from the area for which it meets needs and demands, or that different parts of the area should exchange services for the area as a whole. This sounds rather complex; actually, it merely means that either both State A and State B should help support Institution no. 1, which serves both states, even though located in State A; or that State A, through its Institution no. 1, would exchange services with State B, through its Institution no. 2. By limiting what it attempts to provide, each state would be able to use its educational funds effectively.

The governors were thinking of joint support when they adopted at Asheville, N. C., in the fall of 1947, a resolution agreeing that it was the intent of the conference to provide adequate facilities for higher education for both white and Negro students either within or without the borders of the state in which they resided. They followed this action by signing a compact at Wakulla Springs, Fla., on Feb. 8, 1948, under which the regional education program was to become established upon approval by the legislatures of at least six states. Fourteen legislatures have since approved the compact, establishing a region for educational planning that stretches from Maryland to Texas and from Kentucky to Florida. The compact established the Southern Regional Education Board, composed of the governor and three appointees from each of the states, to develop and direct the program.

The governors' actions were imbued with urgency owing to the impending loss of one of the region's medical schools—Meharry Medical College at Nashville, Tenn. Meharry had had a distinguished history since it was organized in 1876 as Meharry Medical Department of Central Tennessee College. It had graduated its first class in 1887 and had obtained a new charter as an independent medical school in 1915. From its beginning it had been devoted to the training of Negro students and was one of the two medical schools in the United States devoted to this end. A major part of its support in recent years had come from philanthropic foundations. These foundations had informed the institution that they could not continue their grants without assurance that other means of continuing support could be obtained. The trustees of Meharry Medical College, faced with this crisis, had proposed that the institution be taken over by the southern states and operated as a jointly supported and jointly operated institution. Quick action was necessary.

It was fortunate that the crisis at Meharry gave an immediate motivation for action by the southern states, but it was unfortunate that the prominence of Meharry in the early press stories gave the impression that the regional education program was devoted solely to problems of professional education for Negroes. Actually, at no time was the purpose of the program limited to education of Negroes. Because of this misconception, however, some supported the program in the expectation that it would continue the separation of white and Negro students in graduate and professional schools. Because of the same misconception, many violently denounced the program for fear that in some way it would, as they put it, "extend and perpetuate segregation" in graduate and professional education.

We know now that both groups—the supporters who hoped the program would maintain segregation and the opponents who were afraid it would—were wrong. Nine of the member states have admitted Negroes to one or more of their publicly supported professional schools since the regional program has been established. Two states, Kentucky and Texas, came into the compact after their universities had admitted Negroes. If the purpose of the program had been to extend and perpetuate segregation in graduate and professional schools, it has been remarkably unsuccessful. At least nine states should have withdrawn from membership. None has. Actually, although it has taken a long time to prove it, the board has operated on a policy that is neither for nor against segregation. It believes that the institutions are responsible for their own admission policies, over which the Southern Regional Education Board should have neither influence nor control. Any other position on the part of the board would constitute an invasion of an institution's rights and would properly be resented.

A month after the governors signed the compact, educators and governors met at Gainesville, Fla., and took the first steps toward putting the program in operation. They established and incorporated a Regional Council for Education to undertake initial studies prior to the time legislatures could act on the compact. A staff was organized and set to work by September of 1948, and proposals for a specific program in medicine, dentistry, and veterinary medicine were readied for the legislatures to act on in the spring of 1949, when they would also consider the compact. The legislatures did approve the compact and appropriated funds for the operation of the program. The Regional Council was, therefore, discontinued and the Southern Regional Education Board formed in June of 1949. The first students under the program entered the schools in the fall of that year.

That was the "Why." How does the program operate? Essentially, its operation was based on the fairly simple idea of extending the area from which a particular school receives its support; for example, Florida does not have a medical school. Its students were having difficulty in obtaining admissions to medical schools outside the state. Florida agreed, therefore, to pay to schools under contracts $1,500 per student per year for Florida students accepted up to a specific quota. The board's staff negotiated contracts with five institutions, Duke University, Emory University, Vanderbilt University, Meharry Medical College, and Tulane University, to accept Florida students who had been certified as legal residents by the state itself. Florida established a certification committee composed of one representative of each accredited school in the state. This committee reviews the records of the Florida applicants for medical school, excludes on academic grounds only those who are obviously not qualified to meet the requirements of the medical schools, checks the legal residence of each student, and sends a list of certified students, through the board, to each of

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the institutions with which a contract has been made. The student then applies directly to those institutions in which he is interested. The school makes selections in accordance with its own standards and notifies the students. If admitted to a public institution, the student does not have to pay out-of-state fees.

After enrollments are completed, the schools send invoices to the board that list the names of each student enrolled under the contract. The board approves the invoices and forwards them to the states, which, in turn, pay the required amounts to the board. The board then distributes the money to appropriate institutions. In other words, as you can see, the board acts as a clearinghouse, transferring information and funds as required. The program acts as a means of broadening the base of support for the contracting schools.

The contracts were executed between the states and the board, on the one hand, and between the institutions and the board, on the other. Because of this arrangement, a state needed to make only one contract and an institution only one contract. The contracts established the quotas for each state and institution, set the amount

TABLE 1.—*Number of Medical Students Enrolled Under Regional Program*

Institution	1949-50	1950-51	1951-52 *
Duke University	6	11	17
Emory University	19	39	58
Louisiana State University	4	9	8
Medical College of Alabama	..	4	4
Meharry Medical College	97	101	144
Tulane University	11	28	43
University of Tennessee	10	31	37
Vanderbilt University	4	9	15
Total	151	232	326

* Number of students estimated from budget for 1951-52.

of payment, and stated the minimum payment required: three fourths of the total amount under the quota. The contracts are automatically renewable, unless two years' notice is given, but they are contingent on the appropriations of the state legislatures, since without money the contracts would not be very effective. Except at Meharry, the contracts applied first to a single year of the medical school. For Florida, with no medical school, the quotas have been stated in terms of the number of new admissions for the first-year class. For Mississippi, with a two-year medical school, the contracts have applied first to the third year of medical training. The financial crisis at Meharry was of such intensity that the states agreed to make the contract apply to all four years immediately, so that the money available could be large enough to be of substantial help at once.

A number of specific benefits have developed from the contracts. The number of students and, correspondingly, the amount of funds have steadily increased as the classes moved through their appointed terms. The funds and the number of students involved for each of the three years in which the program has been operating in medical training are given in the tables. It can be seen that the program has been large enough to provide substantial support for several institutions, including Meharry Medical College, Emory University, Tulane University, and the University of Tennessee, and has provided smaller amounts for Duke University, Vanderbilt University, and the University of Alabama. The funds have made it possible to continue Meharry and to raise the quality of its program, while the funds for Emory, Tulane, and the

TABLE 2.—*Money Received by Institutions for Medical Education Under Regional Program*

Institution	1949-50	1950-51	1951-52 *	Total
Duke University	$ 9,000	$ 16,500	$ 25,500	$ 51,000
Emory University	28,500	58,500	87,000	174,000
Louisiana State University	6,000	13,500	12,000	31,500
Medical College of Alabama	.....	6,000	6,000	12,000
Meharry Medical College	143,250	151,500	216,000	510,750
Tulane University	16,500	42,000	64,500	123,000
University of Tennessee	30,500	69,000	62,000	161,500
Vanderbilt University	6,000	13,500	22,500	42,000
Total	239,750	370,500	495,500	1,105,750

* Figures taken from 1951-52 budget.

University of Tennessee have helped meet their increasing costs. Some modifications in admissions have also occurred. Meharry Medical College has given preference to students from the southern states. Meharry officials feared the effects of such a change, but they have been pleasantly surprised at the quality of student. Possibly, better-qualified candidates have been encouraged to apply by the establishment of a quota of students from a particular state. Emory has been able to avoid retrenchment in its instructional program. At Tulane the quality of student from Florida has increased since the contract was established to the point that Tulane now admits almost double the number of students in the Florida quota.

States have also received substantial benefits from the program. They have been able to assure places for their students who are qualified for admission. Mississippi, which is conducting a two-year medical school, decided

TABLE 3.—*Money Paid by States for Medical Education Under Regional Program*

State	1949-50	1950-51	1951-52 *	Totals
Alabama	$ 15,000	$ 15,000	$ 22,500	$ 52,500
Florida	76,500	130,500	193,500	400,500
Georgia	16,500	16,500	21,000	54,000
Louisiana	6,000	12,000	15,000	33,000
Maryland	9,000	10,500	10,500	30,000
Mississippi	54,500	117,000	120,500	292,000
North Carolina	18,000	18,000	19,500	55,500
South Carolina	5,250	9,000	15,000	29,250
Tennessee	18,000	18,000	28,500	64,500
Texas	.....	.....	24,000	24,000
Virginia	21,000	24,000	25,500	70,500
Total	239,750	370,500	495,500	1,105,750

* Figures taken from 1951-52 budget.

to admit two classes each year and thereby double its output. The contracts made it possible for Mississippi to find places for this increased output with no difficulty. Florida's governor has been so pleased with the arrangement that he stated at the board meeting in Charleston, S. C., in 1950: "This is the greatest bargain since manna fell on the children of Israel." The program may not be quite such a miracle as the governor's statement suggests,

but many requirements of Florida students for medical training have been met. A by-product value mentioned by both Mississippi and Florida is the student's belief that his state wants him to practice there since it has assumed an obligation for his instruction. The program has not been, and in my opinion should not become, a complete substitute for the medical school requirements of a particular state. The Mississippi legislature and the University of Mississippi are proceeding to establish a four-year medical school at Jackson, because they can demonstrate the school is needed both to provide training for third and fourth year students and to become the capstone of a statewide program in medical care. When this school is completed, Mississippi will need to use the regional program only to supplement its own facilities, not to serve as a substitute for them. Much the same is true in Florida, except that the situation there is not yet clear. As I understand it, the legislature has appropriated some funds for planning a medical school at the University of Florida at Gainesville but has more recently passed another bill, under which the state would pay to the first accredited medical school in Florida the sum of $3,000 per year per Florida student. Eventually, however, Florida will probably build a medical school.

When Florida and Mississippi establish four-year medical schools, every state of the compact area will have within its borders at least one medical school. Every state except Kentucky will have a state-supported medical school. Virginia and Texas will have two state-supported schools. The region, with about a fourth of the nation's population, will have 24, or just about a third, of the four-year medical schools in the nation. The contracts for medical education will probably be substantially reduced as Mississippi and Florida develop four-year medical schools. As that occurs those states will have less reason for helping to support institutions elsewhere. When each state needs and develops a particular educational program there obviously is less need to work out interstate arrangements of any sort.

In what directions then does the future of the program lie? It is clear that there will not be further expansion of the contracts for medical training unless student demand expands suddenly. If that occurs, some states may desire to supplement their own facilities with contracts to add places to the ones already available to their students. A state may meet a portion of its student demand through its own medical school but contract through the board with schools in other states to meet the remainder of the demand that could not be satisfied within the state. Texas now has a quota of students at Meharry Medical College serving to supplement the number of students trained in its own medical schools.

In a field such as public health, student demand and society's need are not great enough to require a school of public health in every state. At present the South is blessed with three public health schools: at Johns Hopkins, the University of North Carolina, and Tulane. These schools may be sufficient to meet the requirements of all the states. Each is suffering from lack of adequate support, and the principle of contract funds, based on a broader area of support, may be a solution to the problem. This possibility will be explored during the spring months. If the situation appears promising, a plan will be presented to the legislature for approval in 1953. Another possibility not yet explored is cooperative effort among medical schools based on the method of exchange of services rather than contracts. The various schools will consider planning research and advanced specializations in line with what is needed in the region. Already forestry schools have taken a look at possibilities in their field. If successful among medical schools, regional planning could create strong offerings in research and specialized phases of the medical field at different points throughout the region, so that the needs of students can be effectively met. Possibilities are limited here only by the imagination and ingenuity of the institutions.

Beyond the medical field the possibilities of regional cooperation in higher education are broad. It appears likely that contracts for services will be a permanent feature of the dental, veterinary, medical, and social work training in the region, because it is highly unlikely that every state in the region will establish schools in these fields. The method of exchange of services has particular applicability to graduate work in the more academic fields, and the board is now exploring the possibilities in such areas as aeronautics, oceanography, political science, statistics, chemistry, pulp and paper, and forestry. In each of these fields, colleges and universities will meet with each other and with representatives of the public and government agencies to work out ways by which each interested institution can provide that part of a total program that it can do best. They will also try to work out new methods of financial support calling upon industry, government, philanthropic foundations, and private donors to contribute to regional programs whose objectives are set by regional and national needs and whose method of cooperation assures the most effective expenditure of funds. This kind of development, the board believes, will help to make higher education a constantly more powerful instrument by which the South may be able to achieve the rich and vigorous life for which its resources and people form the potential.

830 W. Peachtree St.

Antibiotic Therapy.—In attempts to eliminate one pathogenic strain, major changes in the total bacterial flora of the body may occur which have unforeseen results. For instance, when one administers full doses of penicillin or aureomycin or both to eliminate pneumococci or streptococci from some part of the body, these microörganisms may disappear, but an astonishing increase in other organisms which are not sensitive to these agents may occur. Pseudomonas aeruginosa may arise in sufficient numbers to cause very troublesome infections of the urinary tract, meninges, or lungs. E. coli or enterococci may disappear from the urinary tract, but B. proteus or Ps. aeruginosa may take their place, causing an even more persistent infection. Candida albicans may flourish and may cause very persistent infections about the anus, vagina, or oral cavity as the microörganisms sensitive to aureomycin disappear.—P. S. Rhoads, M.D., The Antibiotics—Uses and Abuses, *GP*, February, 1952.

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ESTATE PLANNING FOR PHYSICIANS

PART 2: FUNDAMENTALS, THE YOUNG PHYSICIAN'S FIRST PLAN

W. S. McClanahan, Chicago

This is the second of a series of articles being developed for physicians who are interested in problems relating to economic security in their business and home activities. Other articles on estate planning and insurance will be published in THE JOURNAL *soon.*—ED.

In the first article of this series,[1] we defined estate planning, pointed out the economic changes in recent years that have made it essential to a successful and happy financial life, and examined the physician's special need for professional advice in formulating his financial and estate plans. A logical question here might be, "What are the first steps in estate planning?"

This question can best be answered by looking at the situation of the young professional man, as he starts full-time work in his chosen field. It has been stated that the average physician will be about 28 years of age, with 9 or 10 years of costly education and training behind him, as he enters practice.[2] Let us assume further that he entered practice owing a modest debt to his family for part of his education and office equipment, that he has set up his own practice, and that he is already married. It is obvious that his first needs would be food, shelter, clothing, and the other necessities for himself and his wife. He also must have enough income or funds from other sources to pay his office expenses and maintain his automobile during those difficult months while his patient list is building.

For a time it is going to require close figuring to keep these expenditures within his limited income. If one asked him what plans he had made for the future, he might properly say that he has no time for such luxuries, that he is too busy trying to build up his practice and "to make both ends meet." Yet even in this early stage he has probably started to plan, albeit unconsciously. He may have a small sum put away in his first bank account ("for an emergency"), and he may have his first life insurance policy ("so that my wife would have a little something, if anything happens to me").

FUNDS FOR EMERGENCIES

The young man has already started to plan; he has taken the first steps to insure against two of the hazards that are common to everyone and concern us at every age level—emergencies and premature death. In most family plans a reserve fund to meet emergencies has a high priority and is the first fund set aside from earnings. There have been many articles and whole books written on financial plans for families; each has its own recommended level for emergency reserve funds, ranging from one month's earnings to enough to maintain the family six months on a reduced scale. Each person should analyze his particular situation, preferably in a family conference, decide what his requirements are, and then build his fund up to that level as rapidly as he can and keep it there.

This should not be considered as a vacation fund or a new car fund to be depleted and rebuilt every year or two. It should remain inviolate for the real emergency that may strike without warning. A portion of it should certainly be in cash or a bank account. The balance of it might be in short term bonds or some other form of investment that is readily convertible to cash. The principal requisite of an emergency fund is that it should always be there and should be in cash, or its equivalent, if it is to serve its real purpose.

Having set his personal requirements and created his emergency fund, is the young physician's planning for this hazard completed? No, this fund will have to grow with him. As the years go by there will be many changes that will affect his needs. Earnings will increase, living standards will change, children will be born, and other events will affect family planning. Requirements should be reviewed periodically and the emergency fund should be increased or decreased as conditions change. It is well to state here the first fundamental: Estate planning is not static—it is a continuing activity that ends only when the estate owner and his dependents are gone from the scene.

LIFE INSURANCE

Now let us go back and consider the young physician's provision against that second hazard, premature death. It was stated that he may have his first life insurance policy. Most young men will have acquired at least one policy before they leave school. Often it is purchased and the premiums are paid by a parent until the young man gets started in his profession. It may be rather small, and at best it probably would not begin to compensate the parent for the cost of the young man's education, but it is a start. Let us assume that the young physician has a $5,000 ordinary life insurance policy, purchased by his father and naming the father as beneficiary while he was in school. As the physician entered practice, his father gave the policy to him, he changed the beneficiary to his wife, and assumed the payment of premiums. Does he have enough insurance? Certainly not! How much should he have? This is a question that cannot be answered in the abstract. The needs of each family group are determined by its own aims, desires, hopes, plans, and ability to pay.

Dr. B. L. Riese, addressing a recent graduating class of Northwestern University School of Medicine, told the young physicians that his classmates range in age from 66 to 75 years, that 67% continue in active practice, 7% are disabled, and less than 30% have been able to retire. "If we may make a suggestion," he said, "to the young men now starting out in practice, a suggestion born of long and bitter experience, it would be to buy all the life insurance they can afford to carry, in a sound com-

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1. McClanahan, W. S.: Estate Planning for Physicians: The Business Side of the Physicians' Life, J. A. M. A. **148**: 1401 (April 19) 1952.

2. Dickinson, F. G.: Income Tax Discrimination Against the Professions, J. A. M. A. **142**: 1357 (April 29) 1950.

pany, and out of their surplus to buy bonds and stocks of basic industries, leaving the gold mines to the gamblers."[3]

It should be noted that about 40% of the active physicians in the United States had military service in World War II, and many have retained their National Service Life Insurance. This group has an advantage over others in that they may have up to $10,000 of this insurance on a very low cost basis. Originally this was term insurance, with restricted beneficiary provisions and rigid settlement terms. Amendments to the laws since the war have made it possible to convert this insurance to one of several permanent plans and have liberalized the settlement options available. The physician who has this insurance should consult his life underwriter as to whether to convert to a permanent plan and what settlement option to select. Of course the choice of an option depends on many personal factors, but it should be noted that option 4 (the refund annuity option) is unusually desirable in this insurance. Congress was so liberal in setting the rates that a $10,000 policy settled under this option is about equal to $12,500 in a private insurance company. Regardless of whether this insurance is still on a term basis or converted to a permanent plan, the physician should, by all means, retain it; it is good insurance and can be fitted in well with his estate plan and a sound insurance program.

That brings us to another of the fundamentals of estate planning—particularly for professional men: Life insurance is the foundation of most successful estate plans today. About 86 million Americans now own over 250 billion dollars worth of life insurance in companies with assets totalling over 68 billion dollars. This is a high tribute to the confidence reposed in the institution of life insurance by the average American. For persons whose lifetime accumulations of property will come to them solely in the form of taxable income (salaries, fees, and commissions), life insurance is almost the only sure way to create or build a satisfactory estate. As was pointed out in the previous article, high income taxes, decreasing purchasing power of the dollar, and declining interest rates have taken their toll. The old pattern of saving a portion of earnings, investing it, and reinvesting the income as received will seldom create an estate that is sufficient for all purposes at all times. This may work out well in later life, when the children are grown and family responsibilities are lessened, and when earnings may exceed current needs. But the young physician looks forward to long years of heavy and increasing responsibilities, and his current income provides only for current needs and leaves no excess for an investment program.

Something else is needed, and that something else is life insurance. It is the only asset that multiplies in value immediately at death. It is the only method by which the young man can make sure that his primary plans can be carried out, even if death intervenes long before he has a chance to complete his other plans. For his long range plans (retirement), life insurance and its close associate, annuities, can furnish the retirement income to the physician which Social Security and private pension plans furnish to the business employee.[4]

So the young physician's second step in estate planning should be to enter into a program of purchasing life insurance that will build an adequate insurance estate. The details of how to formulate such a program, what types of insurance it will include, and the dates and amounts of purchases are beyond the scope of this article. The field of modern life underwriting is so broad, the purposes which insurance can serve are so diversified, and the types of policies available are so varied that whole books are written on one phase of the subject. All I can do here is to suggest some general principles of creating an insurance estate as part of an over-all estate plan.

THE LIFE INSURANCE UNDERWRITER

It is at this point that the young physician should, and probably will, first become acquainted with a member of the "estate planning team" mentioned in the previous article. This is the life insurance representative or agent, who is now more commonly referred to in the estate planning field as the "life underwriter" or simply "underwriter." He is an important member of this team and is a good man to know.

Naturally not all life underwriters are equally trained and experienced as insurance technicians, just as they do not possess the same personal traits that mark the sincere and friendly insurance counsellor. Great progress has been made in the past 25 years, however, in the joint efforts of the insurance companies and the underwriters to raise the standards in the insurance sales field.[5] An outstanding example is the growth of the American College of Life Underwriters and its program of education and on the job training, leading to the certificate of Chartered Life Underwriter (known in the estate planning field as C. L. U.).[6] This is coming to be recognized as a professional designation in the insurance field, and may at some future date achieve a standing equal to that of C. P. A. in the accounting field. In addition to this program, many insurance companies have emphasized college education as a prerequisite to joining their sales force, and they engage in extensive programs of home office and branch training before the new man commences actual sales work. Although the number of C. L. U.'s is not large compared to the total insurance sales force today, the trend indicates that in a generation or two a sizeable proportion of the competent underwriters may have earned this professional designation.[7] It is well to remember, however, that life insurance selling is, by its nature, a "soliciting" business and should remain so. Only as the life insurance underwriters continue active solicitation of new business will the Amer-

3. Time and Money, Boston, The Cambridge Associates, 1952.

4. It was noted in the previous article that these two forms of retirement income may provide up to $300 per month for the business employee.

5. One of the principal reasons for the wide acceptance of life insurance in America has been the work of a trained, full-time sales force. In America insurance is "sold." In many other countries insurance is "bought"; that is, the buyer must take the initiative. As a result America, with only 7% of the world's population, owns 75% of the world's life insurance. The insurance salesman can take pride in having helped to make America life insurance conscious.

6. The C. L. U. must qualify under standards of character, knowledge, and experience. The course includes studies in economics, government, sociology, law of insurance, wills, trusts and estates, taxation, banking and credit, corporation finance, and investments. He must pass a series of five comprehensive, written examinations. Over 200 colleges and universities now cooperate in offering these studies and supervising these examinations.

7. Over 4,500 persons have completed the course of training and have received the certificate of C. L. U. since the founding of the college in 1927, and 5,500 others are now taking the examinations. While this is a small segment of the persons engaged in insurance sales, the trend toward professional training is significant (Gregg, Davis W.: Twenty-Five Years of C.L.U., J. Am. Soc. Chartered Life Underwriters **6**: 50 [Dec.] 1951).

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ican family continue its preeminent position as the best insured and protected family group on earth.

The young physician should align himself with a life underwriter early in his practice. It is not difficult to locate and identify a good life underwriter. There are men in every community who have built a solid reputation for technical insurance knowledge, skillful analysis of family needs, honest advice as to what insurance best meets those needs and sincere interest in the financial welfare of their policyholders. These men enjoy a respected place in the business community. Inquiry by the young physician among his older colleagues, his business associates, the bankers, trust officers, and attorneys of the community will place him in touch with the type of life underwriter who can and will become a trusted insurance counsellor.

Having placed himself in the hands of a competent life underwriter, the physician should give him his confidence and his insurance business. Shopping around for bargains or passing his insurance business around on a basis of personal friendships will not build a sound, integrated insurance program. He should disclose to his life underwriter all pertinent facts about his family and financial status, as he would to his banker or attorney. He should seek and accept the advice of this underwriter as to a long range program for acquiring an insurance estate, as to the specific types of policies needed to carry this out and the time when purchases and changes should be put into effect. One of the requisites of a good insurance program is the periodic review of the entire plan by the policyholder and life underwriter and the prompt revision of any part of it to meet changed conditions.

An essential element of a sound insurance program is that it is tailored to meet the specific needs of the individual policyholder. There is no such thing as "the correct plan" for a certain age group, to the exclusion of all other plans. Yet there are certain general principles that all life underwriters follow in constructing an individual plan. As stated above, the young physician will find that his need for insurance protection will be greatest when his funds available to buy it are least adequate. If funds for premium payment were unlimited, it would be simple to lay out a plan for $100,000 or more of permanent protection for the young physician and his family from the day he starts practice. Since realities must be faced, the young man's program is always going to include several compromises. His long range plan will call for purchase of various types of permanent policies, which include both the protection and the investment features. His immediate need is for the most protection he can get for the least cost. Thus the life underwriter may recommend that his first purchases be 5 or 10 year term insurance, which includes no investment features and is convertible to permanent insurance without physical examination. Also frequently recommended is a contract known as a family income policy, which includes elements of both term and permanent insurance. Since term life insurance is expensive if continued longer than necessary, it should be converted to permanent insurance as soon as feasible. If the young physician will take the time to let his life underwriter explain the basic features of the various contracts, and will study them seriously, he can purchase his first insurance intelligently, and thus get the most value for his premium dollars. He will have made a good start on the most important part of his estate plan.

MAKING A WILL

Having made a start on these first two phases of his estate plan, an emergency fund and an insurance program, the young physician should proceed at once to the third phase; he should make a will. This cannot be overemphasized; it is of paramount importance. It is often said in estate planning that a will is the most important document a man will ever sign, unless it is his application for a marriage license. This may sound facetious, but it is literally true. There is no other way in which a person can be sure that his estate, however small, will be distributed according to his wishes at his death. I have not the space here to go into the many compelling reasons why every physician should have a will, or the pitfalls encountered when he dies without a will. These were so ably set out by Judge Waugh (of "the world's busiest court") in THE JOURNAL,[8] that it would be worth while for every physician to read this article again.

It is at this stage of his planning that the young physician will probably become acquainted with the second member of the estate planning team—the lawyer. It might be well to state here the third fundamental of estate planning: Everyone should have a will. Its corollary is the fourth fundamental: Only a lawyer should prepare a will. If the physician lives in a larger community where the banks and trust companies are engaged in estate planning, at this time he may also become acquainted with the third member of the team, the trust officer, who will work with the lawyer in plainning the estate and its future management.

In my experience in assisting with the estate plans of persons of all ages, the commonest objections to making a will raised by the young man are: "my estate is too small," "my estate is very simple—it all goes to my wife," or "my property is all in joint tenancy—I don't need a will." Let us take a few moments to analyze these statements.

"My estate is too small." I have become very skeptical of this statement. Many times a customer has made this statement in the utmost sincerity, and we have then proceeded to list and analyze his assets. Perhaps it turned out that he had only a small bank account, a few savings bonds, some household furniture, an automobile, and a few small life insurance policies. Did he have an estate and need a will? Certainly! It does not take much imagination, in these days of high prices, to translate those few ordinary items into a value of several thousand dollars. One large trust institution embarked on a public education program a few years ago, the theme of which was, "If you have $1,000 you have an estate." This highlights the fact that often the small estate needs the added protection that a well drawn will provides more than the large estate. The small estate simply cannot afford the shrinkage and avoidable loss occasioned by the lack of a will. Or if the husband and wife die together, the proceeds of those few small insurance policies

8. Waugh, W. F.: Wills for Physicians, J. A. M. A. **144**: 842 (Nov. 4) 1950.

may be distributed in a way contrary to the wishes of the insured, unless he has a will. Size of the estate alone does not determine the need for a will. If a person has any property at all and a normal human desire to pass it on to some favored person or group at his death, he needs a will.

"My estate is very simple—it all goes to my wife." If this were literally true, in some situations it might be satisfactory to let the law distribute one's property. It is surprising how many men assume this to be the fact. No state has laws giving all a man's property to his wife in every situation. Most states provide a larger share for the children (even during infancy) than for the wife. Allowing fractional shares of property to descend by law to minor children may make it very difficult for the wife to use the property promptly for the best interests of the children and herself.[9] In many states some types of property (such as real estate) must be shared by the wife with her husband's brothers, sisters, and parents, if there are no children. No, the simplicity of the estate, or the mistaken idea of the estate owner as to who will get it at his death, will not lessen the trouble, expense, and frustration caused by failure to make a will.

"My property is all in joint tenancy—I don't need a will." This is even a commoner sedative to lull the property owner into a false sense of security. It is true that joint tenancy (in those states which recognize it), and tenancy by the entirety (in other states), are valuable methods of owning property in many situations. Lawyers and trust officers often recommend it when all facts are known. It is a simple and inexpensive method of passing title to certain assets, such as the family home, to the wife. But it is essentially a legal device, hedged about with many technical restrictions, and it can incur extra taxes in some situations.[10] A pamphlet published by the Illinois State Bar Association [11] asked the question, "Is joint tenancy a substitute for a will?" The answer given was, "It is in about the same sense that a size 34 suit will fit a man; it will fit some men but not others." In some cases it may defeat the wishes of the estate owner, in some cases it will add considerably to the tax burden of the surviving joint tenant, and it is not a certain device to avoid all death taxes and probate expense. The principal thing that the young physician should remember, as he acquires a bank account, a home, and securities, is that he should take title in joint tenancy only on the advice of his lawyer, after a full disclosure of all the facts.

There are many other reasons given by young men for not having made a will. None of them should be allowed to defer this all important duty. The young physician should not feel self-conscious about going to his lawyer for his first will. Many a man twice his age has sat at my desk and apologetically said, "I just never got around to making a will, but last month my best friend died and left his affairs in a terrible mess, so I decided to make a will right now." In many countries property owners have no choice, or very limited rights, to say who shall get their property at their death. It is a tragedy that in America, where we have the most liberal of laws and the broadest privilege to choose who shall benefit from our property after we are gone, so many people neglect this valuable privilege.[12]

The young physician will find that having his lawyer prepare his will is not a burdensome or time consuming task. When it is done, he will experience a deep sense of satisfaction in knowing that his estate, however small, will be distributed under his will to his dependents and loved ones, according to his own individual plan.

PURCHASING A HOME

Perhaps one more phase of the young physician's estate plan should be mentioned, the purchase of a home. Most persons consider this a major transaction and one of their most valuable assets, although they may not consider it as an investment. This is such a local problem that no specific suggestions of value could be made in an article of this type. Every detail of the transaction will be governed by family status, individual taste, financial ability, size of community, state laws, and local real estate practices. In the smaller communities the physician may buy or build his home before he enters practice. In the larger urban centers he may rent an apartment or house for several years before buying a home of his own.

Twenty years ago there were some "rules-of-thumb" in the real estate business regarding the relation between a person's annual income and the amount he should invest in a home. These varied considerably between different localities and different sized communities. Taking Chicago as an example of a large urban center, it was said that a young man should not pay more than two or three times his annual income for a home. Changes in personal income taxes, in the purchasing power of the dollar, and in methods of home financing (such as the advent of the long-term, monthly payment, F. H. A. insured loan) have played havoc with such rules. Today we are more likely to compare the home buyer's annual income to his "total occupancy costs" for the home, including interest and principal payments on the mortgage, insurance, taxes, heating, repairs, and maintenance. Taking Chicago as an example again, the banks and other lending agencies are likely to advise the young man not to commit himself to pay more than 20% of his annual income for these occupancy costs of his home. The young physician would be wise to consult his local banker about such considerations in his own community before purchasing a home.

A home is a sound investment, but not from the standpoint of income or capital appreciation. Its value lies more in the fact that it brings to the owner a sense of pride, personal satisfaction, family solidarity and belonging to the community. It should be bought whenever the physician's family status makes it desirable and his financial status makes it feasible. A word of caution should be added here: Seek competent advice before taking even the first steps to purchase a home. Real estate is in a class by itself. From the first signature on a con-

9. Local laws of descent of property are the determinants in this situation. In Illinois the wife would inherit one-third and the children two-thirds of the property. A guardianship for the minors would add to the cost of administration and might delay a necessary sale to the detriment of the estate. The physician should consult his attorney about the laws of his state relating to these matters.

10. A further discussion of some of the disadvantages of joint tenancy will be contained in a subsequent article.

11. Wills—Their Importance and Why You Should Have One, Springfield, Ill., Illinois State Bar Association, 1947.

12. Judge Waugh [5] states that in one large metropolitan area 60% of the estates going through the probate court are administered without a will.

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tract to purchase to the final approval of title by a lawyer, it is fraught with special risks to the layman. The local realtor should be consulted as to questions of construction, location, neighborhood trends, appraisals, and value. The local banker should be consulted on methods of payment and financing. Above all the lawyer should be consulted, early in the transaction, as to questions of contracts, deeds, surveys, mortgages, and either an abstract or title guarantee policy.[13] He should act as the coordinator of the entire transaction. A real estate purchase completed without legal advice can be the source of trouble and litigation in future years. The usual fee of the lawyer is a small premium to pay for the assurance that your title is "free and clear of all encumbrances."

There is one more suggestion worthy of consideration by the young physician purchasing his first home, and that is to purchase so-called "mortgage insurance," which will provide the cash to pay the mortgage in the event of his death. Although permanent insurance may be used for this purpose, decreasing term insurance, in which the death benefit is reduced as the mortgage is paid off, is frequently recommended. Many a young widow has been forced to sell her home because she could not keep up the mortgage payments from her limited income after her husband's death. This protection assures her of a home for herself and the children, free of debt. Here again the life underwriter should be consulted to work out the details of such a program.

There are many other transactions that the young physician may enter into in his first years of practice that might be considered as part of his estate plan. There is not space to mention them here. If the young physician has created an adequate emergency fund; has embarked upon a sound insurance program with the advice of his life underwriter; has executed a well-drawn will with the advice of his lawyer; and, perhaps, has purchased a satisfactory home with the advice of realtor, banker and lawyer, he will have made an excellent start on a sound estate plan that should lead to a successful business career. He will have avoided the costly mistakes of many business and professional men that we in the estate planning field are often asked to correct in later years.

605 N. Michigan Ave.

13. These same suggestions apply with equal force to other real estate transactions, including the sale of one home and purchase of another. The Revenue Act of 1951 made some important changes in the treatment of this latter transaction for income tax purposes.

Unnecessary Estrogen Therapy.—Fully half of all women who go through the menopause do not require estrogen therapy. It is unfortunate that nearly every woman in the late forties who complains to her physician of vasomotor and nervous disturbances is given estrogen hypodermically or orally. Even many women in their early forties who still bleed regularly but complain of vague but distressing symptoms are given estrogens. It is a serious mistake to give estrogens to women who have not stopped menstruating and even to some who have had a true menopause, i. e., cessation of bleeding. In most cases, estrogens will have to be administered for years if their use is not restricted and limited to the minimum from the start. Many women can be carried through the trying days of the change of life by encouragement and phenobarbital. And if estrogens must be prescribed there is little need to give them hypodermically.—J. P. Greenhill, M.D., 1951 Year Book of Obstetrics & Gynecology, The Year Book Publishers, Inc., Chicago, p. 524.

COUNCIL ON PHARMACY AND CHEMISTRY

The following abstract of recent nomenclature decisions of the Council is authorized for publication.

R. T. Stormont, M.D., *Secretary.*

NEW GENERIC AND BRAND NAMES RECOGNIZED BY THE COUNCIL

The Council collaborates with manufacturers in the selection of generic and brand names for marketed drug preparations presented for acceptance and also for new products still under development or clinical trial. The last report on such names appeared in The Journal, Nov. 3, 1951, page 950.

The following abstract lists the generic designation, the chemical name, where necessary for information, and the brand name or names simultaneously recognized for the stated firms. In general, a generic name should bear recognizable relation to the chemical name and conform as closely as is consistent with brevity and practicality to existing systems of scientific nomenclature. The chief requirement for a brand name is that it should not be therapeutically suggestive.

Alkavervir for a powdered extract of Veratrum viride alkaloids: Veriloid (Riker Laboratories, Inc.)

Benzoquinonium Chloride for the synthetic compound 2,5-bis-(diethylaminopropylamino)benzoquinone bis-benzyl chloride: Mytolon Chloride (Winthrop-Stearns, Inc.)

Calsulfhydryl for the compound aqueous dispersion of sulfur complexes of calcium polysulfides and thiosulfates containing a labile sulfhydryl group: Hydrosulphosol (E. C. Lientz & Co., Inc.)

Chloromethapyrilene Citrate for N,N-Dimethyl-N′-(2-pyridyl)-N′-(5-chloro-2-thenyl)-ethylenediamine citrate: Chlorothen Citrate (Whittier Laboratories)

Cyclocumarol for the compound 3,4-(2-methyl-2-methoxy-4-phenyl)dihydropyranocoumarin: Cumopyran (Abbott Laboratories)

Gallamine Triethiodide for tri-(diethylaminoethoxy)benzene triethyliodide: Flaxedil Triethiodide (Lederle Laboratories Division, American Cyanamid Company)

Iodopanoic Acid for 3-(3-amino-2,4,6-triiodophenyl)-2-ethyl-propanoic acid: Telepaque (Winthrop-Stearns, Inc.)

Mercaptoarsenol for 2-acetylamino-4-(methylol-cycloethylene-dimercaptoarsine) phenol: Balarsan (Endo Products, Inc.)

Methamexamine for 2-methylamino-4-methylhexane: Naremide (Sharp & Dohme, Inc.)

Monobenzone for the monobenzyl ether of hydroquinone: Benoquin (Paul B. Elder Co.)

Selenium Sulfide: Selsun Sulfide (Abbott Laboratories)

Sodium Carboxymethylcellulose for that derivative of methylcellulose: Thylose Sodium (Jackson-Mitchell Pharmaceuticals, Inc.)

Streptokinase-Streptodornase for a mixture of these two enzymes: Varidase (Lederle Laboratories Division, American Cyanamid Company)

Sulfisozazole and Sulfisoxazole Diethanolamine for 3,4-dimethyl-5-sulfanilamido-isoxazole and the diethanolamine salt: Gantrisin and Gantrisin Diethanolamine Hoffmann-LaRoche, Inc.)

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MEMBERSHIP AND FELLOWSHIP IN THE AMERICAN MEDICAL ASSOCIATION

Some physicians are confused concerning their status as members or fellows of the American Medical Association. This confusion has occurred because prior to 1950 all physicians who were active members of their state medical societies automatically became members of the American Medical Association. More than 70,000 of these members by 1949 had applied for fellowship, which entitled them to receive THE JOURNAL or one of the special journals, and to participate in the scientific activities of the American Medical Association. In 1949 a voluntary assessment was levied on the members of the Association, and in 1950 dues were imposed for the first time. A summary of the changes that have occurred in the membership and fellowship structure of the American Medical Association appears in the Organization Section of this issue of THE JOURNAL. This will explain for any physician who is in doubt what is required now for membership in the Association.

Reprints of the statement in the Organization Section will be available in any quantity for medical oganizations and publications. Inquires should be directed to the Secretary of the Association, Dr. George F. Lull, or to the Director of Records and Circulation, 535 North Dearborn St., Chicago 10.

FOUNDATION'S 1952 CAMPAIGN UNDER WAY

Aiming at a goal of 2 million dollars, the American Medical Education Foundation has launched its 1952 fund-raising campaign. Committees of state and county medical societies have been organized and are at work in almost all states in a concentrated effort that began early in April and will continue until the end of June. The objective of this intensive campaign is to raise as much of the 1952 fund as possible by the end of June so that substantial sums can be made available to the medical schools when they begin their next fiscal year on July 1.

The prospects for this year's fund appear bright. During the first three months of 1952 more individual gifts were received than during the entire year of 1951, even though this year's drive had not officially been initiated.

In establishing the Foundation, the medical profession is pioneering in an effort to find a positive solution to the serious financial problems that beset the nation's medical schools. Already this effort has stimulated new support for the medical schools from lay groups through the National Fund for Medical Education and from the members of the profession itself through newly established alumni funds, local foundations, support at budget hearings before state legislatures, and by other means. A successful campaign this year will add greatly to the real momentum that is being developed for solving the problems of medical education through local and voluntary action.

Physicians are reminded that they may earmark their gifts for a specific school and that the full amount of the gift will be transmitted to the school through the National Fund for Medical Education over and above the school's full share of unearmarked funds raised by the Foundation and the Fund. All expenses of the Foundation's fund-raising effort are being borne separately by the American Medical Association and by the state and county medical societies participating in the drive. Thus the entire amount of all gifts received will be passed on to the medical schools—an unusual feature in fund-raising campaigns.

Physicians who wish to support the Foundation are urged to make their contributions at this time. Contributions should be directed to the officers for the state drive where such drives are being conducted. Where no state campaign is in motion, checks should be sent to the Foundation, 535 North Dearborn Street, Chicago 10.

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DIAGNOSIS OF INFECTIOUS MONONUCLEOSIS

The diagnosis of infectious mononucleosis is now made in the presence of a variety of clinical pictures, both acute and chronic. Often the only laboratory confirmation is the finding of atypical lymphocytes in the peripheral blood. Some observers believe that this is not sufficient evidence and that heterophil agglutinins must also be present before a positive diagnosis can be made. Opinion in the literature is divided on this point.

Many investigators have found negative heterophil agglutinin reactions in a significant proportion of patients with symptoms and blood smears characteristic of infectious mononucleosis. Others have found the agglutination reaction positive in every, or almost every, fully developed case of this disease. There are several possible explanations for this discrepancy, two of which are reviewed by Bender in this issue of THE JOURNAL (page 7). In the first place, the incidence of positive reactions in different series of cases varies according to the investigator's definition of positivity. A worker who regards a titer of 1: 16 as the dividing line between normal and abnormal will find more positive reactions than one who regards a titer of 1: 320 as critical. In the second place, the number of positive reactions encountered depends on the time of performance of the tests. As significant titers of agglutinins may not appear until the end of the first week or later and since they may disappear within two weeks, single tests performed before or after these dates may be negative. In the third place,

the incidence of positive reactions will vary with the criteria the author uses for the admission of patients to his series. If he accepts as bona fide cases only those in which there are positive heterophil agglutination reactions, the incidence in his series can hardly be less than 100%. If, on the other hand, he bases his diagnosis solely on the presence of atypical lymphocytes, he may include in his series patients who actually do not have infectious mononucleosis, since these cells may occur in other diseases. Finally, the percentage of positive agglutination reactions may depend on technical factors. If the tests are performed on refrigerated serum, false positive results may be obtained owing to the presence of cold agglutinins.[1] These reactions disappear on rewarming the serum to 37.5 C. Moreover, false negative reactions may be obtained if the sheep erythrocytes used are of low agglutinability. Keiper [2] and Zarafonetis and Oster [3] have found that the agglutinability of erythrocytes from different sheep varies widely and that cells from an occasional sheep react only slightly with the serum of known cases of infectious mononucleosis. Lesser variations in agglutinability are encountered in cells drawn periodically from the same sheep, and there is some variation following storage of cells.

It is evident that absolute agglutinin titers obtained with different samples of sheep cells have much less significance than is generally believed. Under these circumstances, only a rise in agglutinin titer during the course of the disease can be regarded as significant and then only if all serum specimens are saved and tested simultaneously against one lot of sheep cells of known agglutinability. Since this technique has seldom been used in studies published to date, reports of borderline positive and negative reactions must be interpreted with caution. Variations in agglutinin titers may also be obtained by varying the concentration of cells used in the test.[2] It is obvious that discrepancies in the results obtained by different workers cannot be eliminated until techniques are standardized and specified in published reports.

In support of the argument that neither atypical lymphocytes nor sheep cell agglutinins alone should be accepted as positive evidence of infectious mononucleosis is the fact that neither of these signs is found exclusively in this disease. Abnormal lymphocytes are occasionally seen in a variety of conditions resembling infectious mononucleosis clinically, including infectious hepatitis, primary atypical pneumonia, German measles, measles, acute brucellosis, allergic rhinitis, asthma, migraine, acute sinusitis, pharyngitis, laryngitis, bronchitis, angina pectoris, and coronary thrombosis. Sheep cell agglutinins also occur in a number of conditions other than infectious mononucleosis.[4] They are found in low titers in serum from normal subjects and in higher but reversible titers in serum containing cold agglutinins. They have also been found following injection of horse serum, and in the serum of patients with infectious hepatitis,[5] primary atypical pneumonia,[6] German measles,[7] scarlet fever,[8] polycythemia, various sarcomas, tuberculosis, monocytic leukemia, Hodgkins disease,[9] and other diseases. It is claimed that the reactions encountered in leukemias are probably due to cold agglutinins.[10]

Attempts to differentiate the hematological and serologic reactions occurring in infectious mononucleosis from those occurring in other diseases have not been entirely successful. While the agglutinin titers and atypical cell counts in infectious mononucleosis are usually higher than those occurring in other diseases, this is not always true, so that no absolute quantitative differentiation is possible. Qualitative differentiation of the atypical lymphocytes is said to be aided by supravital staining,[11] but this approach has not been adopted widely. Qualitative differences in the sheep cell agglutinins occurring in different conditions have been described, but these are apparently not invariable. It is stated [12] that: 1. The agglutinins found in infectious mononucleosis are absorbed by ox cells but not by guinea pig kidney. 2. The agglutinins found in normal serum are absorbed by guinea pig kidney but not by ox cells. 3. The agglutinins occurring after horse serum injections are absorbed by both antigens. These tests have proved useful in the differential diagnosis of many cases of infectious mononucleosis, but they have also yielded a number of inconsistent results. Agglutinins from patients with infectious mononucleosis have given the reaction usually seen in normal serum, while agglutinins from patients with serum sickness have given the reaction supposedly characteristic of infectious mononucleosis.[13] Kaufman [9b] found that the agglutinins of several patients with infectious mononucleosis gave the reactions of serum sickness, and at different times in the course of the disease serum from the same patients gave different qualitative reactions with or without changes in agglutinin titer. Other inconsistencies have been found by Wechsler [14] and Liebowitz.[5c] While these occur in only a small proportion of cases and may be due to differences in technique or in the criteria used for the diagnosis of in-

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13. Mason, J. K.: An Ox Cell Haemolysin Test for the Diagnosis of Infectious Mononucleosis, J. Hyg. **49**: 471, 1951.

14. Wechsler, H. F.; Rosenblum, A. H., and Sills, C. T.: Infectious Mononucleosis: Report of an Epidemic in an Army Post, Ann. Int. Med. **25**: 236, 1946.

fectious mononucleosis, they emphasize the fact that qualitative differentiation of various types of heterophil agglutinins is sometimes difficult. In view of the lack of specificity of the laboratory signs of infectious mononucleosis it would seem wise to insist on as many confirmatory tests as possible before making a positive diagnosis. While it is possible that in mild or subclinical cases the stimulation to antibody formation may not be sufficient to produce significant titers of heterophil agglutinins, every effort should be made to detect them in each case by standardized tests performed serially.

RELIEF OF PAIN

Approximately one-half of patients who come to physicians for medical attention complain of pain or discomfort in one form or another. While most patients are not interested in matters pertaining to the physiology and pathology of their illness, they are seldom indifferent to pain or to procedures necessary for obtaining relief therefrom. Fortunately, physicians can relieve pain. This ability is among the greatest attributes of the medical profession; if it did not exist, the skills required to restore the affected person or organ to normal would have little opportunity to prove effective.

Pain can be considered from several points of view. In one, an organic basis is discovered and treated; in another, the cause is undetected and pain is treated as a symptom; and, in a third, the difficulty is psychogenic. Few patients who have been in pain for long periods of time become inured to pain. The longer pain must be endured, the less well it is tolerated. Kolb [1] points out that patients who are in pain as a result of physical disease usually describe their symptoms precisely, signs of physical disease and suffering are commonly evident, there is a demonstrable limitation of movement consistent with the presence of pain, and analgesics provide a full or partial measure of relief. In contrast, patients' complaints are thought to have a psychogenic basis when there are no signs of physical disease, when pain persists long past the usual period of subsidence of a known acute illness or physical injury, and when pain is precipitated and aggravated by discussion of topics emotionally distressing to patients.

Physicians have available to them a number of well-established procedures for relieving pain. These include mechanical means; the use of heat or water to lessen spasm; either a surgical attack on the source of pain or surgical interruption of pain circuits in the peripheral and central nervous systems; the use of anesthetic agents acting locally in the spinal cord or centrally on cerebral function; psychotherapy; and analgesic drugs. At one time the painful conditions for which roentgen therapy was proposed were numerous. Today, the entities for which roentgen rays are prescribed satisfactorily number perhaps no more than a half dozen.[2] Methods of obtaining relief from pain depend on various factors, i. e., the nature of the pain-producing substance, the experience and ability of the attending physician, the general condition of the patient, the physical and geographical circumstances under which treatment is begun, and the availability of different modes of therapy.[3]

Attention has been directed recently to the use of the diagnostic and therapeutic nerve blocks, the former for the purpose of locating pathways of pain and the latter for interrupting pathways of pain either semipermanently or permanently.[4] Greater use is also being made of prognostic nerve blocks, which give the patient the experience of temporary interruption of nerve sensation before the interruption is made permanent or semipermanent. In general, blocking of sensory nerves can provide pain relief for virtually any part of the body.

Pain is frequently a prominent symptom of cardiac disease and sometimes its only manifestation. Pain, in the presence of cardiac disease, may be due to myocardial ischemia or to pericardial irritation and can occur in association with certain diseases of the aortic arch. In the final analysis, a knowledge of pain patterns is the key to the differential diagnosis of pain in, or referred to, the thoracic region.

According to Hammes, drugs that relieve pain are divided into four classes: those that act on the organ or tissue producing the pain; those that act locally to block the conductivity of pain fibers; the true anesthetics that produce unconsciousness, thereby relieving awareness of pain; and the analgesics, which selectively depress the central appreciation areas without loss of consciousness. The drugs of the first group are most desirable, since they act to restore normal function. The analgesics are the most widely prescribed; however, when used promiscuously they constitute a clear and present therapeutic danger, for such practice encourages lax diagnosis on the part of overly busy physicians. Actually, when the precise reason for pain remains undetermined, prescribing an analgesic should be considered to be but a temporary, humane expedient and not an end in itself. There is little doubt that, when analgesic drugs are employed on a rational basis, physicians will come nearest to fulfilling with credit that phase of medical practice which, at least to the patient and his family, is of prime importance—the relief of pain.

COURSE IN ELECTROCARDIOGRAPHY

A short course in basic electrocardiography will be conducted at the Chicago Headquarters during the week prior to the Annual Meeting of the American Medical Association, which is sponsoring the course. The instructors will be leading electrocardiologists of midwestern and southern universities. The course will emphasize the place of the electrocardiogram in the diagnosis and management of heart disease and the harm that may result from improper interpretation. Any member of the American Medical Association is eligible to attend the series of free lectures. Further information will be found on page 68 of this issue of THE JOURNAL.

1. Kolb, L. C.: Pain as a Psychiatric Problem, J. Lancet **72**: 50, 1952.
2. Leddy, E. T.: Analgesic Effect of Roentgen Rays, J. Lancet **72**: 55, 1952.
3. Hammes, E. M., Jr.: Pain Relieving Drugs, J. Lancet **72**: 67, 1952.
4. Pender, J. W., and Lundy, J. S.: Diagnostic and Therapeutic Nerve Blocks, J. Lancet **72**: 76, 1952.

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ORGANIZATION SECTION

REFERENCE COMMITTEES OF HOUSE OF DELEGATES

The Speaker of the House of Delegates of the American Medical Association has appointed delegates to serve on the reference committees of the House at the Chicago Session as follows:

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PAUL A. DAVIS, SECTION ON GENERAL PRACTICE
CARL A. GROTE, ALABAMA
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TELEVISION TO OPEN DOORS OF MEDICAL MEETING

For the first time, through the medium of television, physicians who are unable to attend the annual American Medical Association convention will be able to see at first-hand what is happening. The 101st Annual A. M. A. Convention will be held in Chicago, June 9-13.

Two half-hour, coast-to-coast telecasts of the convention are planned. As the nation's top medical authorities report on the very latest developments in the field of science and medicine to about 14,000 colleagues attending the meeting, mobile television cameras will transmit the news to the rest of the nation.

The programs, to be carried over the NBC television network on Tuesday evening, June 10, and at another date to be announced later, will be sponsored by Smith, Kline and French Laboratories, in cooperation with the A. M. A. The telecasts were conceived by Smith, Kline and French as part of its pioneering in the use of television for medical teaching.

The telecasts, which will be conducted on a strictly scientific and educational level, will present some of the highlights of the 300 scientific exhibits to be displayed at Navy Pier. Phy-

sicians watching a color television program of an operation, and the newest methods of life-saving, symposiums on heart and blood vessel diseases, obesity and diabetes, and numerous other interesting features will be among the presentations.

"These historic telecasts, besides transmitting important medical news to the physician at home and to his patients, will serve to demonstrate that the doctor's quest for life-saving knowledge never ends," said Dr. George F. Lull, Chicago, secretary and general manager of the A. M. A.

"An M.D. degree doesn't automatically give the doctor a healing touch. He must work and sweat to keep up with advancing science. His education is never completed. These programs will show one of the ways he continues to learn.

"The public should not expect a magician's show of medical miracles. Rather, they should expect a view of solid, useful medical progress which will ultimately benefit them."

These telecasts mark a milestone in the dynamic partnership of television and medicine, it was pointed out by C. Mahlon Kline, chairman of the board of the pharmaceutical firm, who added:

"Three years ago our inauguration of color television for medical teaching resulted in an entirely new approach to instruction at medical meetings. The surgical theater, the medical clinic, the doctor and the patient were brought into the meeting by television.

"Now, as the next logical step, television brings the medical meeting to the doctors who cannot attend the meeting and to the public, which is so vitally concerned with the progress revealed at these sessions."

COURSE IN BASIC ELECTROCARDIOGRAPHY

The Board of Trustees of the American Medical Association takes pleasure in inviting members of the Association to attend a course in basic electrocardiography at A. M. A. Headquarters, 535 North Dearborn Street, Chicago, June 3-6, 1952.

As seating accommodations are limited, registration for the course is necessary. Candidates will be considered in order of the time and date of mailing of their applications. Entrance cards will be mailed to successful applicants. There will be no fee for attendance. The subjects and lecturers are:

JUNE 3

Dr. Franklin D. Johnston, University of Michigan, General Chairman

MORNING: What the electrocardiogram really is and its proper place in the diagnosis and management of heart disease.

AFTERNOON: Discussion of different types of electrocardiographic apparatus and important points relative to the technique for taking the proper records. Brief discussion of the electrophysiologic basis of electrocardiography.

DR. FRANKLIN D. JOHNSTON

JUNE 4

MORNING: The normal electrocardiogram—Discussion of the basic waves, important intervals, and criteria for normality in limb and precordial leads. The value of esophageal leads and the current status of spatial vectorcardiography.

DR. GEORGE E. BURCH
Tulane University

AFTERNOON: The use of the electrocardiogram in the cardiac arrhythmias.

DR. LOUIS N. KATZ
Michael Reese Hospital

JUNE 5

MORNING: The use of the electrocardiogram in estimation of cardiac hypertrophy. Intraventricular block. Abnormalities of the T waves (not including those due to myocardial infarction).

DR. GORDON B. MYERS
Wayne University

AFTERNOON: The use of the electrocardiogram in the diagnosis of angina pectoris and myocardial infarction. Electrocardiographic findings in pulmonary infarction.

DR. FRANCIS F. ROSENBAUM
Marquette University

JUNE 6

MORNING: Question and answer period. Informal discussion.

DR. JOHNSTON
DR. BURCH
DR. KATZ
DR. MYERS
DR. ROSENBAUM

Note: Problem electrocardiograms of registrants may be presented for discussion during the fourth day.

Arrangements under auspices of the Committee on Research, Paul L. Wermer, M.D., Secretary.

CHANGES IN THE MEMBERSHIP AND FELLOWSHIP STRUCTURE OF THE AMERICAN MEDICAL ASSOCIATION

Before 1949. Between the years 1913 and 1949, all physicians who were active members of their state society were nondues-paying members of the American Medical Association. Of the 144,211 members of the A. M. A. in June, 1949, a total of 77,723 were listed as fellows. Fellows paid dues to the A. M. A. and received THE JOURNAL, or one of the special journals if they so elected.

1949. The House of Delegates of the A. M. A. assessed all members of the A. M. A. $25.00, but this assessment was not compulsory. This was the only assessment made.

1950. There was no assessment in 1950; however, for the first time membership dues were established, the amount being $25.00 per year. If these dues were not paid by the end of the year, the member was dropped for nonpayment; before he could be reinstated, it was necessary for him to pay the delinquent year's dues. The 1950 dues did not include a subscription to THE JOURNAL. A member in 1950, again through the payment of fellowship dues, received THE JOURNAL, or he could subscribe to it separately.

1951. The membership dues in the A. M. A. in 1951 were $25.00 and for the first time included a subscription to THE JOURNAL. Fellowship dues were reduced, but a subscription to THE JOURNAL was no longer included.

1952. Dues for membership during this year are the same as for 1951. There are no fellowship dues, and fellowship cards are not being issued. Fellowship may be abolished after the Annual Meeting of the A. M. A. in June, 1952.

The following summary will further clarify the changes from 1949 to 1952:

	Membership in the American Medical Association	Fellowship in the American Medical Association	Subscription Price of THE JOURNAL
	Membership dues in the A.M.A. never included fellowship dues. Membership dues have been payable only through the county and state societies.	Fellowship in the A.M.A. was dependent on membership in the state and county societies. The A.M.A. fellowship dues were payable directly to the A.M.A. and were in addition to the membership dues.	Since Jan. 1, 1951, the price of THE JOURNAL has been included in membership dues; rates below for 1951 and 1952 are for nonmembers and laymen. Anyone may subscribe to THE JOURNAL.
1949	Assessed $25.00 but payment not compulsory	Dues of $12.00 included THE JOURNAL	$12.00
1950	Dues of $25.00 did not include THE JOURNAL	Dues of $12.00 included THE JOURNAL	$12.00
1951	Dues of $25.00 included THE JOURNAL	Dues of $5.00 did not include THE JOURNAL	$15.00
1952	Dues of $25.00 include THE JOURNAL	No fellowship dues for 1952	$15.00

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MEDICAL NEWS

ARIZONA

State Medical Meeting at Phoenix.—The annual meeting of the Arizona Medical Association was held April 30 to May 3 in Phoenix under the presidency of Dr. Harry T. Southworth of Prescott. Among the papers presented by out-of-state speakers were the following:

Chronic Gastritis, Hale F. Shirley, San Francisco.
Anesthetic Problems and Emergencies, Scott M. Smith, Salt Lake City.
Cancer Detection—The Physicians Responsibility; Minimum Requirements for a Cancer Detection Examination; Realistic Appraisal of Its Value, Ian G. Macdonald, Los Angeles.
Recent Advances in Therapeutics, L. Maxwell Lockie, Buffalo.
Prevention of Coronary Thrombosis, William P. Thompson, Los Angeles.
Cor Pulmonale, Osborne A. Brines, Detroit.
Congenital Hips in the Practice of Every Physician, Harold E. Crowe, Los Angeles.
Isonicotinic Acid Hydrazine in Treatment of Tuberculosis, Edwin R. Levine, Chicago.
Thoracoplasty with Subscapular Paraffin Pack, William M. Lees, Chicago.

COLORADO

Clinical Day in Children's Diseases.—A clinical day for physicians interested in children's diseases will be sponsored by St. Francis Hospital and the University of Colorado School of Medicine May 21 at St. Francis Hospital, Colorado Springs. Dr. Mary S. Goodwin, consultant, Public Health Service, Federal Security Agency, will discuss "Diagnosis and Treatment of Congenital Syphilis."

CONNECTICUT

Psittacosis.—Dr. James C. Hart, Connecticut Department of Health, reports that six parakeets, found to be on sale and illegally brought into the state on Feb. 28, have been confiscated by the Milford Health Department. The birds were sent to the Virus and Rickettsial Laboratory in Montgomery, Ala., where the psittacosis virus was noted in five. The parakeets had been purchased in Chicago.

IDAHO

Outbreak of Typhoid.—Dr. Terrell O. Carver, Idaho Department of Public Health, has reported preliminary information on an outbreak of typhoid in Bonner County. In January, three cases appeared in one family in Sandpoint. Two of these were confirmed by bacteriological culture and the other by clinical symptoms. In February, two cases were reported from Priest River. The city of Sandpoint empties raw sewage into the Pend Orielle River and until recently the town of Priest River had obtained its water supply from the same river without chlorination. The three cases in Sandpoint have been traced to a chronic carrier, also a member of the family, who resides in Cusick, Wash.

ILLINOIS

Illinois Association of Blood Banks.—A panel discussion on the techniques and problems of blood banking will be featured at the meeting of the Illinois Association of Blood Banks in the Hotel Sherman, Chicago, on the afternoon of May 13. The panel will cover processing, donor selection and screening, grouping, Coombs test, reactions, and small community blood bank problems.

Lectures on Emotional Reactions.—A lecture on "Emotional Reactions to Fertility and Sterility" will be delivered by Dr. Boris B. Rubenstein, research associate at the Institute for Psychoanalysis and at the Institute for Psychosomatic and Psychiatric Research and Training of Michael Reese Hospital, Chicago, at 8 p. m. May 7 at the North Shore Health Resort, 225 Sheridan Road, Winnetka. This is one of a weekly series of lectures on emotional reactions to stress that is being offered by that institution.

Anesthesiologists Meeting.—The annual meeting of the Illinois Society of Anesthesiologists will be held at the Hotel Sherman, Chicago, May 12-13 under the presidency of Dr. Bryce K. Ozanne, Moline. Clinical demonstrations will be held from 8 to 11:30 a. m. on both days in various Chicago hospitals. Out-of-state speakers will include Dr. John E. Steinhaus, Madison, Wis., "Reactions to Local Anesthetic Drugs," Dr. John W. Pender, Rochester, Minn., "Care of the Patient During Mitral Commissurotomy," and Drs. Jacob J. Jacoby, Columbus, Ohio, and Vergil K. Stoelting, Indianapolis, whose subjects were not announced.

Society News.—The annual luncheon of the Illinois chapter of the American Academy of Pediatrics will be held May 13 in the Bal Tabarin room of the Hotel Sherman, Chicago. All physicians interested in pediatrics are invited to attend.——The Illinois Obstetrical and Gynecological Society will hold its annual meeting in the Hotel Sherman, Chicago, May 12 under the presidency of Dr. Ralph R. Loar, Bloomington. Dr. Virginia K. Pierce, New York, will present a paper on "Dilatation and Curettage as an Office or Outpatient Procedure." A panel discussion on "Results of a Two Year Hospital Survey by Districts" will be given by Drs. Joseph K. Hanson, Moline; Henry A. Hartman, Kankakee; Mary L. Newman, Jacksonville, and Andrew J. Hurter, Urbana, with Dr. Worling R. Young, Geneseo, as moderator.

State Medical Meeting in Chicago.—The Illinois State Medical Society will hold its annual meeting at the Hotel Sherman, Chicago, May 13-15 under the presidency of Dr. C. Paul White, Kewanee. Out-of-state speakers include the following:

Clifford F. Gastineau, Rochester, Minn., Electrolyte and Water Balance.
Richard M. Shick, Rochester, Minn., Dangers and Pitfalls of Dicumarol Therapy.
Henry L. Williams, Rochester, Minn., Treatment of Headaches.
John M. Caldwell, Washington, D. C., Preventive Psychiatry for the Physician.
Fay K. Alexander, Philadelphia, Diagnosis of Duodenal Ulcers in Children.
Cecil Stricker, Cincinnati, Diabetes Mellitus: An Orientation.
Harry F. Dowling, Washington, D. C., Problems in Practical Use of Antibiotics.
Charles L. Buxton, New York, Limitations of Hormones in Gynecology.
Claude J. Hunt, Kansas City, Mo., Trends in Surgical Treatment of Some Gastrointestinal Lesions.
Wolfgang W. Zuelzer, Detroit, Hemolytic Anemia in Children.
Hart E. Van Riper, New York, Rehabilitation—Prescription for Living.

A symposium on nutrition will be held May 14 and one on geriatrics May 15.

Chicago

Lecture on Professional Courtesy.—The second Arthur William Stillians Lecture of the Metropolitan Dermatological Society of Chicago will be given at its annual meeting May 14 by Dr. Erwin Paul Zeisler, professor of dermatology, Northwestern University Medical School, who will speak on "The Question of Professional Courtesy."

KANSAS

State Tumor Conference.—The Wichita County Medical Society Cancer Clinic will present the State Tumor Conference on May 15 at Midwestern University, Wichita Falls. Physicians are invited to attend the one day program, for which there is no registration fee. The speakers are as follows:

Arthur P. Stout, New York, Lesions of the Breast.
Juan A. del Regato, Colorado Springs, Colo., Treatment of Carcinoma of Cervix.
Claude F. Dixon, Rochester, Minn., Carcinoma of Rectum: Radical Surgical Treatment.

Physicians are invited to send to this department items of news of general interest, for example, those relating to society activities, new hospitals, education and public health. Programs should be received at least three weeks before the date of meeting.

KENTUCKY

Surgical Society to Meet.—The annual meeting of the Kentucky Surgical Society will be held May 24 at French Lick, Ind. Dr. Henry W. Cave of New York, guest speaker, will discuss "Management of Massive Hemorrhage from the Upper Gastrointestinal Tract."

New Child Health Foundation.—The main field of endeavor of the Kentucky Child Health Foundation, which is closely affiliated with the University of Louisville School of Medicine, will be in medical education, with stress on the promotion of better understanding of health and disease in children. The latest information on all aspects of child health, preventive, diagnostic, and curative, will be brought to the attention of the members of the University of Louisville School of Medicine faculty to further undergraduate instruction and postgraduate seminars.

Rural Health Conference.—The first state wide conference on rural health, organized by the state Rural Health Council, will convene at the Brown Hotel, Louisville, beginning at 2 p. m. May 7 and ending at noon, May 8. Guest speakers include Aubrey D. Gates, field director, American Medical Association Council on Rural Health; Sewall Milliken, chief of public health education division, Ohio State Department of Health; and Frank J. Welch, Ph.D., dean of the College of Agriculture of the University of Kentucky. Dr. Franklin S. Crockett, Lafayette, Ind., chairman of the American Medical Association Council on Rural Health, and Mrs. Charles W. Sewell, Otterbein, Ind., past president of the American Farm Bureau Federation Women's Organization, will talk at the dinner meeting at 6:30 p. m. The topics presented will cover community problems relating to rural health.

MARYLAND

Society News.—The spring scientific meeting of the Maryland Academy of General Practice will be held May 15 at the Hotel Alexander in Hagerstown. Medical films in color and sound, from 10 a. m. to 12 noon, will deal with urinary tract infections, cervicitis, and anticoagulant therapy. The afternoon session, from 1 to 5 p. m., will be devoted to a symposium on carcinoma presented by Drs. Richard H. Chamberlain, Isidor S. Raydin, William T. Fitts Jr., Thomas E. Machella, Franklin L. Payne, Douglas P. Murphy, Robert C. Horn Jr., Joseph P. Atkins, and Julian Johnson, all of the University of Pennsylvania School of Medicine, Philadelphia.

MASSACHUSETTS

Society News.—The Norfolk District Medical Society will hold its annual dinner May 7 at 6 p. m. at the Harvard Club of Boston. Dr. Paul B. Magnuson, chairman of the President's Commission on the Health Needs of the Nation, will speak on "Mental Ramblings on Medical Care."

MICHIGAN

Dedicate St. John Hospital.—The new five million dollar St. John Hospital in suburban Detroit was dedicated March 9. This first new general hospital to be built under the Greater Detroit Hospital Plan will be operated by the Sisters of St. Joseph. It has 266 beds and 68 bassinets, with plans for future addition of 120 beds. There are four major and two minor operating rooms with space reserved for two more. The pediatric section will accommodate 58 children. Dr. Charles J. Jentgen, a graduate of the University of Michigan, has been named medical director.

Restoration of Beaumont Memorial.—Through a resolution adopted at its last annual session, the Michigan State Medical Society has undertaken the restoration of the William Beaumont Memorial. It is proposed that the replica be built in the American Fur Company Store on Mackinac Island, the scene of the meeting on June 19, 1822, of Dr. William Beaumont and the wounded Alexis St. Martin, which led to Dr. Beaumont's epochal studies on the action of the stomach's digestive processes. It is hoped that the memorial will be completed in 1952, so that it may commemorate the 130th anniversary of Dr. Beaumont's discoveries. Contributions are being made on a voluntary basis. Names of all contributors will be inscribed permanently in the Beaumont Memorial.

MINNESOTA

Art Exhibit.—The Minnesota Physicians' Art Association's third annual art exhibit will be held at the time of the meeting of the Minnesota State Medical Association, May 26-28, in the Minneapolis Auditorium. All art pieces should be sent to arrive between May 15 and May 21.

MISSOURI

Food Poisoning.—Dr. J. Earl Smith, St. Louis commissioner of health, has reported six cases of food poisoning that occurred in persons eating in a large hotel. Chocolate eclairs were eaten by those who became ill. Insanitary methods of handling this food and lack of refrigeration were demonstrated.

Annual Memorial Lecture.—Menorah Hospital Medical Center of Kansas City gave its annual memorial lecture on April 29. Dr. Jacob Lerman, associate physician at the Massachusetts General Hospital and clinical associate in medicine, Harvard Medical School, Boston, spoke on "Recent Advances in Thyroid Physiology and the Treatment of Thyroid Disease."

Annual Leo Loeb Lecture.—The annual Leo Loeb Lecture was presented April 17 at the Washington University Medical School by Dr. Paul B. Beeson, professor and chairman of the department of medicine, Emory University School of Medicine, Atlanta, who spoke on "Some Promising Leads in the Study of Infectious Diseases." The Leo Loeb Lectureship is sponsored by Mu chapter of Phi Beta Pi medical fraternity.

Basic Ophthalmology Course.—The department of ophthalmology of Washington University School of Medicine is forming its 1952-1953 class for the basic course in ophthalmology, to begin Sept. 15, 1952. Tuition is $800. The course is approved by the Veterans Administration. Instruction includes 393 hours of didactic work and 759 hours of clinical work. The course is limited to 12. Correspondence should be addressed to Dr. Richard G. Scobee, director of graduate training in ophthalmology, 640 S. Kingshighway Blvd., St. Louis 10.

Personals.—Dr. Walter C. Alvarez, Chicago, professorial lecturer at the University of Illinois, on March 31 gave the annual William H. Vogt lecture sponsored by Alpha Kappa Kappa fraternity of St. Louis University School of Medicine, St. Louis. ——Dr. Goronwy O. Broun, professor of internal medicine at St. Louis University School of Medicine, has given permission to the American Foundation for the Blind to record his book "Medical Essentials for Students of the Professions Allied to Medicine" for the use of the blind.——Dr. Arthur W. Proetz, professor of clinical otolaryngology at the Washington University School of Medicine, St. Louis, has been invited to deliver the annual Semon Lecture in London, which is a memorial to Sir Felix Semon, one of the distinguished laryngologists of the Victorian era.——Dr. Robert Dean Woolsey, instructor in surgery, St. Louis University School of Medicine, will deliver a report on "Review of 300 Cases of Protruded Intervertebral Disks Treated Surgically" before the International College of Surgeons meeting in Madrid, Spain, May 22.

MONTANA

Society Election.—At the recent semiannual meeting of the Montana Academy of Oto-Ophthalmology, Dr. Fritz D. Hurd, Great Falls, was elected president and Dr. Harvey L. Casebeer, Butte, secretary.

Medical-Surgical Conference.—On May 19-20 the Yellowstone Valley Medical Association will hold its annual Medical-Surgical Conference at Billings. Among the guest speakers will be Drs. Alton Ochsner, New Orleans, Elexious T. Bell, Minneapolis, Edgar V. Allen, Rochester, Minn., and Ernest M. Hammes, St. Paul.

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NEW MEXICO

Annual State Medical Meeting.—The annual session of the New Mexico Medical Society will be held May 8-10 in Elks Hall, Carlsbad, under the presidency of Dr. Coy S. Stone of Hobbs. Out-of-state speakers include:

Mynie G. Peterman, Milwaukee, Fever Convulsions.
Curtis H. Burge, Houston, Roentgen Diagnosis of Gastrointestinal Lesions.
Paul Dudley White, Boston, Medical Practice 40 Years Ago and Now.
William F. Mengert, Dallas, Texas, Obstetrical Hemorrhage.
Oswald S. Lowsley, New York, Prostatic Surgery and Kidney Surgery.

The Woman's Auxiliary to the New Mexico Medical Society will meet May 9.

NEW YORK

Shigellosis.—The New York State Department of Health has reported an outbreak of bacillary dysentery, which occurred in an institution. In a group of 250 children, 46 became ill. All parts of the institution were involved in the outbreak. Shigella sonnei type of organisms were recovered from the stools of the patients.

Nu Sigma Nu Lecture.—Dr. William Dock, professor of medicine at the State University College of Medicine, New York, gave the annual Herman G. Weiskotten Lecture for Mu chapter of Nu Sigma Nu fraternity on April 22 at the State University College of Medicine at Syracuse. He spoke on "Anatomic and Metabolic Considerations in Coronary Artery Disease."

New York City

Course in Surgical Anatomy.—This course will be given at Cornell University Medical College June 2-28 as a full time course, five and a half days a week. It will consist of an intensive review of surgical anatomy, with demonstrations and dissection, and will be especially designed for candidates for the American Board of Surgery. Dr. Ernest W. Lampe will be in charge. Tuition is $200 and the registration is limited to 25. Inquiries may be directed to the Office of the Dean, Cornell University Medical College, 1300 York Ave., New York 21.

Postgraduate Pediatric Course.—The New York University Post-Graduate Medical School will hold a seminar on the rehabilitation of children May 19-23 at the Institute of Physical Medicine and Rehabilitation of the New York University-Bellevue Medical Center. Courses, to be held Monday through Friday from 9 a. m. to 5 p. m., will encompass the following subjects: poliomyelitis, cerebral palsy, spina bifida, muscular dystrophy, and cardiac conditions. Tuition fee is $30. Applications may be addressed to Dr. George G. Deaver, Director, Children's Division, Institute of Physical Medicine and Rehabilitation, 400 E. 34th St., New York 16.

Course at Cancer Center.—The pediatric department of the Memorial Center for Cancer and Allied Diseases announces a three day course May 21-23 for pediatricians, general practitioners, and health officers. The course includes established methods in diagnosis and management of tumors, Hodgkins disease, leukemia, and reticuloendotheliosis in childhood. Demonstrations, examinations of children in pediatric, surgical, chemotherapy, and radiotherapy clinics, ward rounds, and seminars are offered under the direction of the staffs of the Memorial Center and Sloan-Kettering Institute for Cancer Research. The fee is $35. Information may be obtained from the Director of Pediatric Service, Memorial Center, 444 E. 68th St., New York.

NORTH CAROLINA

University Alumni Day.—Two hundred and fifty alumni attended the first annual medical alumni day March 5. Participants in a roundtable discussion on the educational service functions of the medical school to the state included Drs. Samuel H. Proger, professor of medicine at Tufts College Medical School, Boston; Charles M. Caravati, associate professor of clinical medicine at the Medical College of Virginia, Richmond; Kinloch Nelson, professor of clinical medicine at the Medical College of Virginia, and John A. Ferrell, Raleigh, executive secretary of the North Carolina Medical Care Commission.

Personals.—Dr. John F. Fulton, Sterling Professor of the History of Medicine at Yale University, delivered the first Ross Herman Jennings Bryson Memorial Lecture at the University of North Carolina School of Medicine, Chapel Hill, on March 28, on "History of Neurology in the 17th and 18th Centuries."——Dr. William P. Richardson, currently research professor of public health administration and head of the department of field training in the University of North Carolina School of Public Health, has been appointed professor of preventive medicine and assistant dean in charge of continuation education.——Dr. David A. Young, superintendent of the North Carolina Hospitals Board of Control, has been named clinical professor of psychiatry at the University of North Carolina.

Postgraduate Courses.—Duke University announces postgraduate courses to be given June 16-19. Dr. Ralph V. Platou, Tulane University of Louisiana School of Medicine, New Orleans, will present papers on "Prenatal Influences," "Birthmarks and Moles," "The Tuberculous Child," and "Congenital Disturbance of Bone Formation," and will participate in roundtable discussions on "Accidents in Children" and "Epilepsy." Presentations by Duke faculty members will include:

Jerome S. Harris, Congenital Heart Disease.
Angus M. McBryde, Prematurity.
Kenneth L. Pickrell, Common Plastic Surgical Problems in Children.
J. Lamar Callaway, Some Dermatological Problems in Children.
Susan C. Dees, The Allergic Child.
Leslie B. Hohman, The Problem Child.
Wilburt C. Davidson, Cancer in Children.
Arthur H. London, Common Pediatric Problems.

Ward rounds will be given on the various services each afternoon. Registration fee is $25. Rooms are available in the university dormitory at $2 a day.

PENNSYLVANIA

Pennsylvania Doctors in Service.—A total of 409 Pennsylvania doctors have been commissioned as medical officers in the Armed Forces and most of them are now serving. Dr. Francis F. Borzell of Philadelphia, chairman of the state advisory committee to the Selective Service System, reports that in no more than six areas has the taking of doctors placed a hazard on the health of the community.

State Radiological Society.—The annual meeting of the Pennsylvania Radiological Society will be held at Bedford Springs May 16-17. The program will open with a film reading session under Dr. Paul G. Bovard, Tarentum. Dr. Francis F. Borzell, Philadelphia, will speak on "The Structure of the A. M. A." Twelve papers are to be presented and followed by discussion. Dr. Jesse T. Littleton, Sayre, will speak by invitation on "The Thymus."

Child Research Clinic.—The Child Research Clinic of the Woods Schools, Langhorne, will hold its annual spring conference May 20 from 10 a. m. to 4 p. m. "Understanding the Exceptional Child" will be the topic discussed by Seymour B. Sarason, Ph.D., professor of psychology, Yale University, New Haven, Conn.; Dr. Leo Kanner, director of the Children's Psychiatric Service, Harriet Lane Home for Children, Johns Hopkins Hospital, Baltimore; Arthur S. Hill, chief, exceptional children and youth, Federal Security Agency, Washington, D. C.; Clara Savage Littledale, editor, *Parents' Magazine*, and Katharine G. Ecob, author. Those interested in attending the conference or in receiving copies of the proceedings may address A. Ralph Carli, Ed.D., director, Child Research Clinic, The Woods Schools, Langhorne.

Course in Reading Electrocardiograms.—A special course in electrocardiography designed to teach general practitioners the fundamentals involved in reading electrocardiograms will be held in the nurses' home of Westmoreland Hospital, Greensburg, under the sponsorship of the commission on graduate education of the Medical Society of the State of Pennsylvania. The dates for the lectures are May 15, 22, 29, and June 5, 12, 19, and 26. The faculty will include Drs. Charles W. Smith, Constantine P. Faller, and Kenneth E. Quickel, all of Harrisburg Hospital; Dr. John B. Levan, St. Joseph Hospital, Reading, and Dr. Thomas

M. Durant, Philadelphia. Dr. Elmer Highberger Jr. of Greensburg is local director of the program. Enrollment may be made by mailing a check for $35 to the Commission on Graduate Education, 230 State St., Harrisburg.

Society News.—The annual joint meeting of the Diplomates Association of Berks County Physicians and the Reading Eye, Ear, Nose and Throat Society was held Feb. 20 in Reading. Dr. Howard T. Karsner, medical research advisor to the Bureau of Medicine and Surgery, Department of the Navy, Washington, D. C., spoke on "Modern Directions of Medical Investigation." The following officers of the Diplomates Association were elected for the ensuing year: Dr. William P. Jennings, president, Dr. John B. Levan, president-elect, and Dr. James E. Landis, secretary, all of Reading. Preceding the regular meeting, an organization meeting of the newly-formed Southeastern Pennsylvania Chapter of the American College of Surgeons was held. The following officers were elected: Dr. William L. Estes Jr., Bethlehem, president, Dr. Frank G. Runyeon, Reading, vice-president, and Dr. Irvin G. Shaffer, Reading, secretary.

Pittsburgh

Personal.—Dr. Daniel C. Braun, Library, Pa., co-chairman of the Commission on Industrial Health and Hygiene of the Medical Society of the State of Pennsylvania, has been appointed medical director of the Industrial Hygiene Foundation and a senior fellow of the Mellon Institute. He will also serve on the staff of the University of Pittsburgh Graduate School of Public Health as the lecturer on occupational health.

Course in Anesthesiology.—The University of Pittsburgh School of Medicine, section of anesthesiology, announces a postgraduate symposium on the "Basic Sciences Related to Anesthesiology" in cooperation with the departments of anesthesiology of the St. Francis, Allegheny General, and Mercy hospitals. This course will be held June 2-6 from 9 a. m. to 6 p. m. Registration fee is $25. Particulars may be obtained from the Chairman of the Committee on Graduate Medical Education, University of Pittsburgh School of Medicine, 3941 O'Hara St., Pittsburgh 13.

SOUTH DAKOTA

State Medical Meeting at Sioux Falls.—The South Dakota State Medical Association will hold its annual meeting at the Cataract Hotel, Sioux Falls, May 18-20 under the presidency of Dr. David A. Gregory of Milbank. Dr. Earl O. Latimer, Chicago, will speak on "Surgery of the Gallbladder and Biliary Tract" and "Treatment of Varicose Veins." Dr. George B. Logan, Rochester, Minn., will speak on "Treatment of Children Having Asthma" and "Obstructions of the Upper Respiratory Tract in Children." Other out-of-state speakers will include the following:

John W. Cline, San Francisco, President of the American Medical Association, Medicine Today.
Harold Gifford, Omaha, Postoperative Care of Eye Patients 25 Years Ago and Now.
Harvey S. Allen, Chicago, Hand Surgery.
Russell D. Herrold, Chicago, Antimicrobial Therapy in Urology.
Wesley W. Spink, Minneapolis, Treatment of Human Brucellosis.
James C. Cain, Rochester, Minn., Treatment of Duodenal Ulcers.
H. Marvin Pollard, Ann Arbor, Mich., Present Management of Peptic Ulcer.

TENNESSEE

Narcotic Violation.—Dr. William Alexander Thompson, Chattanooga, pleaded guilty in the United States District Court at Chattanooga on Nov. 14, 1951, to an indictment charging violation of the Federal narcotic law. On Feb. 21 his sentence was suspended, and he was placed on probation for two years.

Personal.—Donald B. Zilversmit, Ph.D., Memphis, assistant professor of physiology, University of Tennessee Medical Units, received a medal from Queen Juliana of the Netherlands for services in the Dutch Army during World War II.

UTAH

Annual Surgical Meeting.—The annual meeting of the Ogden Surgical Society will be held under the presidency of Dr. George M. Fister of Ogden on May 21-23 at the Orpheum Theatre, Ogden. Collaborating in a symposium on "Acute Abdomen" at 3 p. m. on Thursday will be Drs. J. Garrott Allen, Chicago; Albert H. Aldridge, New York; John L. Emmett, Rochester, Minn.; Raymond W. McNealy, Chicago; I. S. Ravdin, Philadelphia, and Eugene A. Stead Jr., Durham, N. C. Dr. Alton Ochsner, New Orleans, will serve as moderator. Dr. John W. Cline of San Francisco, President of the American Medical Association, will deliver an address on "Problems Confronting American Medicine in the Immediate Future."

WEST VIRGINIA

Society News.—The annual meeting of the West Virginia Academy of Ophthalmology and Otolaryngology will be held at the Greenbrier, White Sulphur Springs, May 12-13 under the presidency of Dr. Arthur C. Chandler of Charleston. Out-of-state speakers will be Dr. Peter A. Pastore of Richmond, Va., who will present a paper on "Otitis Media and Mastoiditis Today," and Dr. John G. Bellows of Chicago, who will discuss "Senile Changes in the Crystalline Lens."

Petition for Osteopathic Injunction.—A petition was filed early in March in the circuit court of Wyoming County, asking for an injunction prohibiting Glenn E. Cobb, an osteopath of Oceana, from practicing medicine and surgery. The petition cites three specific instances in which Cobb administered drugs or performed an operation and sets forth that Cobb is not licensed to practice medicine and surgery in West Virginia. The filing of the petition follows an opinion, handed down a few months ago by the attorney general, in which he held that the present law prohibits osteopaths from administering drugs and performing surgery. The petition was signed by the 11 members of the Medical Licensing Board and by 5 doctors of medicine in their individual capacities. The case was docketed for hearing by the Wyoming County circuit court at the April term.

GENERAL

Goiter Association Meeting.—The annual meeting of the American Goiter Association was held in St. Louis May 1-3 under the presidency of Dr. Willard O. Thompson of Chicago. Thirty-seven papers were presented, and eight were read by title.

Society for Pediatric Research.—This society will hold its annual meeting at the Hotel Chamberlin, Old Point Comfort, Va., May 5-7 under the presidency of Dr. Horace L. Hodes, New York. According to the preliminary program, 39 papers will be presented and 57 read by titles.

Society News.—The annual meeting of the Association of American Physicians will be held in Chalfonte-Haddon Hall Hotels, Atlantic City, N. J., May 6-7 under the presidency of Dr. Oswald H. Robertson, Chicago. A series of 36 papers will be presented, and 18 will be read by title. Dr. Ralph H. Major of Kansas City, Mo., will speak at the dinner on Tuesday.

Pediatrics Meeting.—The area meeting of the American Academy of Pediatrics will be held at the Hotel Statler, Washington, D. C., May 22-24 under the presidency of Dr. Warren W. Quillian, Coral Gables, Fla. In a panel discussion on problems of current interest in neonatal pediatrics, May 22 at 9:45 a. m., physiological aspects will be discussed by Dr. Clement A. Smith and clinical considerations by Dr. Stewart H. Clifford, both of Boston; pathological aspects by Dr. Edith L. Potter, Chicago, and public health aspects by Dr. Leona Baumgartner, New York.

General Practice Awards.—Dr. Charles E. McArthur, M and R Award Committee chairman of the American Academy of General Practice, recently presented the first year's awards, an engraved plaque together with a check for $1,000, to Dr. J. DeWitt Fox of Washington, D. C., for his paper on "ACTH and Cortisone—Miracle Therapy or Medical Tool?" and to Dr. David G. Miller Jr., Morgantown, Ky., for his paper on "Bites and Stings." These articles appeared in *GP*, the official organ of the academy.

Gordon Research Conferences.—The Gordon Research Conferences on vitamins and metabolism, sponsored by the American Association for the Advancement of Science, will be held from June 16 to Aug. 29 at Colby Junior College, New London,

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N. H. The conferences are planned to stimulate research in universities, research foundations, and industrial laboratories through scheduled lectures and free discussion groups. Requests for attendance at the conferences should be addressed to W. George Parks, Ph.D., Director, Department of Chemistry, University of Rhode Island, Kingston, R. I., before May 15.

Annual Urological Meeting.—The Western Section of the American Urological Association will hold its annual meeting under the presidency of Dr. Paul A. Ferrier, Pasadena, Calif., on May 19-22 at the Hotel Huntington in Pasadena. Guest speakers will be Drs. William W. Scott, professor of urology at Brady Urological Institute, Baltimore, and Rubin Flocks, professor of urology at the University of Iowa, Iowa City. The winners of the Joseph F. McCarthy Award will be announced and the prize winning essay read at one of the scientific sessions. The social program will include a golf tournament, sightseeing, dinner dance, and theatre party.

American Laryngological Association.—The annual meeting of this association will be held at the Royal York Hotel, Toronto, Canada, May 23-24 under the presidency of Dr. H. Marshall Taylor of Jacksonville, Fla. Those speaking by invitation include:

Fredrick T. Hill, Waterville, Me., and Irving I. Goodof, Lewiston, Me., Branchiogenic Carcinoma.
Oliver E. Van Alyea and Carl D. Makart, both of Chicago, Rhinolith—Case Report.
Howard C. Ballenger and John J. Ballenger, both of Winnetka, Ill., Vacuum Frontal Sinusitis. Absorption of Air from the Frontal Sinus. Experimental Study on Dogs.

American Psychoanalytic Association.—This association will hold its annual meeting at the Chalfonte-Haddon Hall Hotels, Atlantic City, N. J., May 8-11 under the presidency of Dr. Robert P. Knight, Stockbridge, Mass. Those speaking by invitation include the following:

Peter H. Knapp, Boston, The Ear, Listening and Hearing.
Bruno Bettelheim, Ph.D., Chicago, Initiation Rites in Relation to Menstruation and Child Bearing.
David Rapaport, Ph.D., Stockbridge, Mass., Attempt to Systematize Fragments of the Psychoanalytic Theory of Affects.
Kurt Goldstein, New York, Effect of Brain Damage on the Personality.
Eugene B. Brody, and Frederic C. Redlich, New Haven, Conn., Response to Humor as Indication of Ego Function in Schizophrenic Patients Before and After Lobotomy.
Louis Linn, New York, Trauma and Denial.

Electroencephalographic Meeting.—The annual meeting of the American Electroencephalographic Society will be held at the Hotel Claridge, Atlantic City, N. J., May 10-11 under the presidency of Dr. James L. O'Leary of St. Louis. On Saturday at 9 p. m. after the annual dinner, Dr. John C. Lilly and Ruth Cherry of the Johnson Foundation, University of Pennsylvania, Philadelphia, will deliver an invitational address on "Criteria for the Parcelation of the Cortical Surface into Functional Areas." A symposium on "EEG in Relation to Psychiatry" will be held Sunday at 9:30 a. m. under the chairmanship of Hudson Hoagland, Ph.D., of Shrewsbury, Mass. Participants and their topics will be as follows:

Walter R. Ingram, Ph.D., Iowa City, Brain Stem Mechanisms and Behavior.
Paul D. MacLean, New Haven, Conn., Some Psychiatric Implications of Physiological Studies in the Fronto-Temporal Portion of the Limbic System (Visceral Brain).
Denis Hill, London, England, EEG Studies in Episodic and Psychotic Behavior.
Donald B. Lindsley, Ph.D., Los Angeles, Psychological Phenomena and EEG.
David M. Rioch, Rockville, Md., Resumé: Clinical and Experimental Considerations.

Careers in Service to the Handicapped.—A brochure on "Careers in Service to the Handicapped" has been prepared by the Easter Seal Society to help young people secure information about positions in the fields of rehabilitation of the handicapped. Information from which the manual was prepared was supplied by the American Physical Therapy Association, the American Occupational Therapy Association, the American Speech and Hearing Association, and the International Council for Exceptional Children. It is jointly published by the National Society for Crippled Children and Adults and the National Foundation for Infantile Paralysis, with the cooperation of the Office of Vocational Rehabilitation of the Federal Security Agency. Young people choosing rehabilitation as a career will find available choice jobs in every section of the country. The National Society for Crippled Children and Adults will distribute, free of charge, more than 23,000 copies of "Careers in Service to the Handicapped" to public and parochial school systems; in addition, copies will be given to every college and university throughout the United States. After the initial distribution, individual copies will be available at $0.50 each.

Aero Medical Association.—This association at its meeting in Washington, D. C., in March installed Dr. William R. Stovall of Washington, D. C., as president and chose as officers for the coming year: Rear Admiral Bertram Groesbeck Jr., MC, USN, Washington, D. C., president-elect; Dr. Armand Robert, Paris, France, Dr. Percy B. Wiltberger, Columbus, Ohio, Dr. Alberto Hurtado, Lima, Peru, Dr. Harold B. Dye, Merriam, Kan., and Dr. Wilbur R. Franks, Toronto, Canada, vice presidents; and Dr. Thomas H. Sutherland, Marion, Ohio, secretary-treasurer. The Longacre Award, established in 1947 for outstanding contributions in psychological or psychiatric aspects of aviation medicine, was presented to Sir Frederic Bartlett, Cambridge University, England. The Theodore C. Lyster Award, established in 1947 for outstanding contributions in the general field of aviation medicine, was presented to Dr. Kenneth A. Evelyn, Montreal, Canada. A special feature of the Honor's Night Dinner was the presentation by Major General Harry G. Armstrong, surgeon general, USAF, and outgoing president of the association, of specially embroidered flight surgeons' wings to Dr. Conrad Berens, New York, probably the first flight surgeon, and Dr. Louis H. Bauer, Hempstead, N. Y., founder of the Aero Medical Association. The wives of members in attendance officially formed the Wives' Wing of the Aero Medical Association to support the efforts of their husbands in the advancement of aviation medicine.

FOREIGN

International Congress of Sports Medicine. — This congress under the auspices of the State Secretariat for Technical Instruction and for Sports for Young Persons and of the International Federation of Sports Medicine will be held in Paris May 30 to June 1 under the presidency of Prof. Chailly-Bert. Information may be obtained from Dr. Collet, president of the Comité d'Organisation du IXième Congrès de Médecine Sportive, Comité National des Sports, 4, rue d'Argenson, Paris 8ième, France.

Summer Jobs in Israel.—The Jewish Agency for Palestine offers summer jobs to medical students and x-ray and laboratory technicians who have finished three years of college study and to young medical postgraduates. During their three months' stay in Israel, they will be placed in various medical institutions throughout the country, where they will be able to exchange valuable experience with their colleagues in Israel. The agency guarantees accommodations and will provide all the necessary living expenses during the stay. The only expense to be incurred by the students will be round trip fare to Israel, which amounts to about $600. Information may be obtained from the Coordinator, Israel Summer Programs, Jewish Agency for Palestine, 16 E. 66th St., New York 21.

CORRECTIONS

Gastric Polyps.—In the paper on this subject in THE JOURNAL, March 29, 1952, page 1093, in the sixth line under case 7, the hemoglobin should have been 7.15 gm. per 100 cc. and in the fourth line of the second paragraph in this case report the hemoglobin level should have been 9.01 gm. per 100 cc.

Influence of Alcohol on Auto Driving.—In the item by this title in the letter from Sweden in THE JOURNAL, April 12, 1952, page 1357, the blood alcohol level data, stated in terms of per cent, all differ from the correct values by a factor of 10. For example, in the last line of the first paragraph the figure should be 0.035 and 0.040. The other levels mentioned in this item should similarly be divided by 10 to obtain the correct figures.

MEETINGS

American Medical Association, Chicago, June 9-13. Dr. George F. Lull, 535 North Dearborn St., Chicago 10, Secretary.

AMERICAN ACADEMY OF PEDIATRICS, Areal Meeting, Hotel Statler, Washington, D. C., May 22-24. Dr. E. H. Christopherson, 636 Church St., Evanston, Ill., Executive Secretary.

AMERICAN ACADEMY OF TUBERCULOSIS PHYSICIANS, Chicago, June 7. Dr. Oscar S. Levin, P. O. Box 7011, Denver, Secretary.

AMERICAN ASSOCIATION FOR THORACIC SURGERY, Dallas, Texas, May 8-10. Dr. Paul C. Samson, 2938 McClure St., Oakland 9, Calif., Secretary.

AMERICAN ASSOCIATION OF GENITO-URINARY SURGEONS, Seaview Country Club, Absecon, N. J., June 19-21. Dr. Norris J. Heckel, 122 South Michigan Ave., Chicago 3, Secretary.

AMERICAN ASSOCIATION ON MENTAL DEFICIENCY, Hotel Bellevue-Stratford, Philadelphia, May 26-31. Dr. Neil A. Dayton, P. O. Box 96, Willimantic, Conn., Secretary.

AMERICAN BLOOD IRRADIATION SOCIETY, Conrad Hilton Hotel, Chicago, June 7-8. Dr. H. T. Lewis, 5230 Center Ave., Pittsburgh, Secretary.

AMERICAN BRONCHO-ESOPHAGOLOGICAL ASSOCIATION, Royal York Hotel, Toronto, Canada, May 20-21. Dr. Edwin N. Broyles, 1100 North Charles St., Baltimore 1, Secretary.

AMERICAN COLLEGE OF CHEST PHYSICIANS, Congress Hotel, Chicago, June 5-8. Mr. Murray Kornfeld, 112 East Chestnut St., Chicago, Executive Secretary.

AMERICAN COLLEGE OF SURGEONS, SECTIONAL MEETINGS:
Toronto, Canada, Royal York Hotel, May 15-17. Dr. Stuart D. Gordon, 170 St. George St., Toronto 5, Canada, Chairman.

AMERICAN DIABETES ASSOCIATION, Drake Hotel, Chicago, June 7-8. Dr. J. A. Reed, 11 West 42d St., New York 36, Secretary.

AMERICAN ELECTROENCEPHALOGRAPHIC SOCIETY, Hotel Claridge, Atlantic City, N. J., May 10-11. Dr. John A. Abbott, Massachusetts General Hospital, Boston 14, Secretary.

AMERICAN FEDERATION FOR CLINICAL RESEARCH, Haddon Hall, Atlantic City, N. J., May 4. Dr. Stewart Wolf, 525 East 68th St., New York 21, Secretary.

AMERICAN GERIATRICS SOCIETY, Hotel LaSalle, Chicago, June 5-7. Dr. Malford W. Thewlis, 25 Mechanic St., Wakefield, R. I., Secretary.

AMERICAN GYNECOLOGICAL SOCIETY, The Homestead, Hot Springs, Va., May 12-14. Dr. John I. Brewer, 104 South Michigan Ave., Chicago, Secretary.

AMERICAN HEARING SOCIETY, Chicago, June 28. Mrs. Francis E. Lee, 817 14th St. N.W., Washington 5, D. C., Secretary.

AMERICAN LARYNGOLOGICAL ASSOCIATION, Royal York Hotel, Toronto, Canada, May 23-24. Dr. Louis H. Clerf, 1530 Locust St., Philadelphia 2, Secretary.

AMERICAN LARYNGOLOGICAL, RHINOLOGICAL AND OTOLOGICAL SOCIETY, Royal York Hotel, Toronto, Canada, May 20-22. Dr. C. Stewart Nash, 277 Alexander St., Rochester 7, N. Y., Secretary

AMERICAN MEDICAL WOMEN'S ASSOCIATION, Chicago, June 8. Dr. Irma Henderson-Smathers, 610 Medical Bldg., Asheville, N. C., Corresponding Secretary.

AMERICAN NEUROLOGICAL ASSOCIATION, Hotel Claridge, Atlantic City, N. J., May 8-10. Dr. H. Houston Merritt, 710 West 168th St., New York 32, Secretary.

AMERICAN OPHTHALMOLOGICAL SOCIETY, Hot Springs, Va., June 5-7. Dr. Maynard C. Wheeler, 30 West 59th St., New York 19, Secretary.

AMERICAN OTOLOGICAL SOCIETY, Royal York Hotel, Toronto, Canada, May 18-19. Dr. John R. Lindsay, 950 East 59th St., Chicago 37, Secretary.

AMERICAN PEDIATRIC SOCIETY, Hotel Chamberlin, Old Point Comfort, Va., May 7-9. Dr. Alms C. McGuiness, 237 Medical Laboratories, Univ. of Pennsylvania, Philadelphia 4, Secretary.

AMERICAN PROCTOLOGIC SOCIETY, Milwaukee, June 4-7. Dr. Stuart T. Ross, 131 Fulton Ave., Hempstead, L. I., N. Y., Secretary.

AMERICAN PSYCHIATRIC ASSOCIATION, Atlantic City, N. J., May 12-16. Dr. R. Finley Gayle Jr., 6300 Three Chopt Rd., Richmond 21, Va., Secretary.

AMERICAN PSYCHOANALYTIC ASSOCIATION, Chalfonte-Haddon Hall, Atlantic City, N. J., May 8-11. Dr. LeRoy M. A. Maeder, 1910 Rittenhouse Square, Philadelphia 3, Secretary.

AMERICAN RADIUM SOCIETY, Chicago, June 8. Dr. John Wirth, 635 Herkimer St., Pasadena 1, Calif., Secretary.

AMERICAN RHEUMATISM ASSOCIATION, Conrad Hilton Hotel, Chicago, June 6-7. Dr. William H. Kammerer, 33 East 61st St., New York 21, Secretary.

AMERICAN SOCIETY FOR CLINICAL INVESTIGATION, Atlantic City, N. J., May 5. Dr. William M. M. Kirby, Univ. of Washington School of Medicine, Seattle 5, Secretary.

AMERICAN SOCIETY FOR THE STUDY OF STERILITY, Chicago, June 7-8. Dr. Walter W. Williams, 20 Magnolia Terrace, Springfield 8, Mass., Secretary.

AMERICAN THERAPEUTIC SOCIETY, Blackstone Hotel, Chicago, June 5-8. Dr. Oscar B. Hunter Jr., 915 Nineteenth St. N.W., Washington 6, D. C., Secretary.

AMERICAN TRUDEAU SOCIETY, Hotel Statler, Boston, May 26. Dr. John D. Steele, 1790 Broadway, New York 19, Secretary.

AMERICAN UROLOGICAL ASSOCIATION, Chalfonte-Haddon Hall, Atlantic City, N. J., June 23-26. Dr. Charles H. deT. Shivers, Boardwalk National Arcade Bldg., Atlantic City, N. J., Secretary.

ASSOCIATION OF AMERICAN PHYSICIANS, Atlantic City, N. J., May 6-7. Dr. Henry M. Thomas Jr., 1201 North Calvert St., Baltimore 2, Secretary.

CATHOLIC HOSPITAL ASSOCIATION OF THE UNITED STATES AND CANADA, Cleveland, May 26-29. Rev. John J. Flanagan, S.J., 1438 South Grand Blvd., St. Louis 4, Director.

GEORGIA, MEDICAL ASSOCIATION OF, Atlanta-Biltmore Hotel, Atlanta, May 12-14. Dr. David H. Poer, 875 West Peachtree St. N.E., Atlanta, Secretary.

IDAHO STATE MEDICAL ASSOCIATION, Sun Valley, June 15-18. Dr. Robert S. McKeon, 305 Sun Bldg., Boise, Secretary.

ILLINOIS STATE MEDICAL SOCIETY, Hotel Sherman, Chicago, May 13-15. Dr. Harold M. Camp, 224 South Main St., Monmouth, Secretary.

MAINE MEDICAL ASSOCIATION, Samoset Hotel, Rockland, June 22-24. Mr. W. Mayo Payson, 142 High Street, Portland 3, Executive Secretary.

MASSACHUSETTS MEDICAL SOCIETY, Hotel Statler, Boston, May 20-22. Dr. H. Quimby Gallupe, 22 Fenway, Boston 15, Secretary.

MEDICAL LIBRARY ASSOCIATION, Lake Placid Club, Lake Placid, N. Y., June 24-27. Miss Caroline Riechers, 1758 West Harrison St., Chicago 12, Secretary.

MINNESOTA STATE MEDICAL ASSOCIATION, Minneapolis, May 26-28. Dr. B. B. Souster, 496 Lowry Medical Arts Bldg., St. Paul 2, Secretary.

MISSISSIPPI STATE MEDICAL ASSOCIATION, Jackson, May 13-15. Mr. Roland B. Kennedy, 508 First Federal Bldg., Jackson, Executive Secretary.

NATIONAL TUBERCULOSIS ASSOCIATION, Copley Plaza and Statler Hotels, Boston, May 26-30. Mr. Kemp D. Battle, 1790 Broadway, New York 19, Secretary.

NEBRASKA STATE MEDICAL ASSOCIATION, Cornhusker Hotel, Lincoln, May 12-15. Dr. R. B. Adams, 1315 Sharp Bldg., Lincoln 8, Secretary.

NEW JERSEY, MEDICAL SOCIETY OF, Haddon Hall, Atlantic City, May 19-21. Dr. Marcus H. Greifinger, 315 West State St., Trenton 8, Secretary.

NEW MEXICO MEDICAL SOCIETY, Carlsbad, May 8-10. Dr. L. G. Rice Jr., 221 West Central Ave., Albuquerque, Secretary.

NEW YORK, MEDICAL SOCIETY OF THE STATE OF, Hotel Statler, New York, May 12-16. Dr. Walter P. Anderton, 292 Madison Ave., New York 17, Secretary.

NORTH CAROLINA, MEDICAL SOCIETY OF THE STATE OF, Hotel Carolina, Pinehurst, May 5-7. Dr. Millard D. Hill, 203 Capitol Club Bldg., Raleigh, Secretary.

NORTH DAKOTA STATE MEDICAL ASSOCIATION, Fargo, May 10-13. Dr. E. H. Boerth, 221 Fifth St., Bismarck, Secretary.

OGDEN SURGICAL SOCIETY, Orpheum Theater, Ogden, Utah, May 21-23. Dr. George M. Fister, Ogden, Utah, President.

OHIO STATE MEDICAL ASSOCIATION, Cleveland, May 20-22. Mr. Charles S. Nelson, 79 East State St., Columbus 15, Executive Secretary.

OKLAHOMA STATE MEDICAL ASSOCIATION, Oklahoma City, May 19-21. Mr. R. H. Graham, 1227 Classen St., Oklahoma City, Executive Secretary.

RHODE ISLAND MEDICAL SOCIETY, Providence, May 6-8. Dr. Morgan Cutts, 106 Francis St., Providence 3, Secretary.

SOCIETY FOR INVESTIGATIVE DERMATOLOGY, Hotel Sherman, Chicago, June 7-8. Dr. Herman Beerman, 255 South 17th St., Philadelphia 3, Secretary.

SOCIETY FOR PEDIATRIC RESEARCH, Old Point Comfort, Va., May 5-6. Dr. Sydney S. Gellis, 300 Longwood Ave., Boston 15, Secretary.

SOCIETY FOR VASCULAR SURGERY, Chicago, June 8, Dr. George D. Lilly, 331 Ingraham Bldg., Miami 32, Fla., Secretary.

SOCIETY OF BIOLOGICAL PSYCHIATRY, Hotel Claridge, Atlantic City, N. J., May 11. Dr. George N. Thompson, 1136 West Sixth St., Los Angeles 17, Secretary.

SOUTH CAROLINA MEDICAL ASSOCIATION, Ocean Forest Hotel, Myrtle Beach, May 13-15. Dr. N. B. Heyward, 120 West Cheves St., Florence, Secretary.

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SOUTH DAKOTA STATE MEDICAL ASSOCIATION, Sioux Falls, May 18-20. Dr. L. J. Pankow, 302 First National Bank Bldg., Sioux Falls, Secretary.

SOUTHERN OREGON MEDICAL SOCIETY, Roseburg, May 13. Dr. F. C. Adams, 1435 Esplanade St., Klamath Falls, Secretary.

TEXAS MEDICAL ASSOCIATION, Dallas, May 4-7. Dr. Sam N. Key Sr., 700 Guadalupe St., Austin 3, Secretary.

THE ENDOCRINE SOCIETY, Palmer House, Chicago, June 5-7. Dr. Henry H. Turner, 1200 North Walker St., Oklahoma City 3, Secretary

UPPER PENINSULA MEDICAL SOCIETY, Country Club, Iron Mountain, Mich., June 27-28. Dr. E. Theodore Palm, 412 Superior Ave., Crystal Falls, Mich., Secretary.

WYOMING STATE MEDICAL SOCIETY, Nobel Hotel, Lander, June 5-7. Dr. Glenn W. Koford, 2020 Carey Ave., Cheyenne, Secretary.

INTERNATIONAL

AUSTRALASIAN MEDICAL CONGRESS, Melbourne Victoria, Australia, Aug. 22-30. Dr. C. H. Dickson, Medical Society Hall, 426 Albert St., East Melbourne, Victoria, Australia, General Secretary.

COMMONWEALTH AND EMPIRE HEALTH AND TUBERCULOSIS CONFERENCE, Central Hall, London, England, July 8-13. Dr. J. H. Harley Williams, Tavistock House North, Tavistock Sq., London, W.C.1, England, Secretary General.

CONGRESS OF THE INTERNATIONAL DIABETES FEDERATION, Leyden, Netherlands, July 7-12. Dr. F. Gerritzen, 33, Prinsegracht, The Hague, Netherlands, Secretary.

EUROPEAN CONGRESS OF CARDIOLOGY, University of London, Bloomsbury, W.C.1, England, Sept. 10-12. Dr. K. Shirley Smith, 35 Wimpole St., London, W.1, England, Secretary.

EUROPEAN SOCIETY OF CARDIOVASCULAR SURGERY, Strasbourg, France, Oct. 3-4. Sir James Learmonth, Department of Surgery, University New Buildings, Edinburgh 8, Scotland.

INTERAMERICAN CARDIOLOGICAL CONGRESS, Buenos Aires, Argentina, Aug. 31-Sept. 7. Dr. Blas Moia, Larrea 1132, Buenos Aires, Argentina, Secretary-General.

INTER-AMERICAN CONGRESS OF PUBLIC HEALTH, Havana, Cuba, Sept. 27-Oct. 1. Pan-American Sanitary Bureau, 2001 Connecticut Ave., Washington, D. C

INTER-AMERICAN CONGRESS OF RADIOLOGY, Mexico City, Mexico, Nov. 2-8. Dr. Guido Torres Martinez, Marsella No. 11, Mexico, D.F., Secretary-General.

INTERNATIONAL COLLEGE OF SURGEONS, Madrid, Spain, May 20-24. Dr. Max Thorek, 850 West Irving Park Road, Chicago, Ill., U. S. A., Secretary-General.

INTERNATIONAL CONGRESS OF BIOCHEMISTRY, Paris, France, July 21-27. Prof. Jean Courtois, 4, Avenue de l'Observatoire, Paris 6e, France, Secretary.

INTERNATIONAL CONGRESS OF COMPARATIVE PATHOLOGY, Madrid, Spain, May 4-11. Prof. Carda-Aparici, Calle Fernando VI.8, Madrid, Spain, Secretary.

INTERNATIONAL CONGRESS OF DERMATOLOGY AND SYPHILOLOGY, London, England, July 21-26. Dr. Gordon B. Mitchell-Heggs, 5, Lisle St., London, W.C.2, England, General Secretary.

INTERNATIONAL CONGRESS OF DIETETICS, Royal Tropical Institute, Amsterdam, The Netherlands, July 7-11. Miss Diane J. Ten Haaf, Educational Bureau of the Nutritional Council, 42 Koninginnegracht, The Hague, Netherlands, General Secretary.

INTERNATIONAL CONGRESS ON DISEASES OF THE CHEST, Rio de Janeiro, Brazil, Aug. 24-30. Mr. Murray Kornfeld, 112 East Chestnut St., Chicago 11, Illinois, Executive Secretary.

INTERNATIONAL CONGRESS OF HAEMATOLOGY, Mar del Plata, Argentina, Sept. 21-26. Dr. Carlos Reussi, Anchorena 1710, Buenos Aires, Argentina, Secretary.

INTERNATIONAL CONGRESS OF HEALTH TECHNICIANS, Palais de la Mutualite, Paris, France, June 9-14. Secretariat General, 6 Square Desaix, Paris XVe, France.

INTERNATIONAL CONGRESS OF THE HISTORY OF MEDICINE, Nice-Cannes, France, and Monaco, Sept. 8-18. Dr. F. A. Sondervorst, 124 Avenue des Allies, Louvain, Belgium, Secretary-General.

INTERNATIONAL CONGRESS OF INTERNAL MEDICINE, Friends House, London, N.W.1, Eng. Sept. 15-18. Sir Harold Boldero, 12 Pall Mall East, London, S.W.1, England, Secretary.

INTERNATIONAL CONGRESS ON MEDICAL RECORDS, London, England, Sept. 7-12. Miss Gwen Perkins, 120 C Street S.E., Washington, D. C., Chairman.

INTERNATIONAL CONGRESS OF MEDICINE AND SPORT, Paris, France, May 29-June 1. Prof. Chailley-Bert, 1 rue Lacretelle, Paris 15e, France, Chairman.

INTERNATIONAL CONGRESS ON NEUROPATHOLOGY, Rome, Italy, Sept. 8-13. Dr. Armando Ferraro, 722 W. 168th St., New York, N. Y., U. S. A., Secretary General.

INTERNATIONAL CONGRESS OF PHYSICAL MEDICINE, London, England, July 14-19. Dr. A. C. Boyle, 45, Lincoln's Inn Fields, London, W.C.2, England, Hon. Secretary.

INTERNATIONAL CONGRESS OF PHYSIOPATHOLOGY OF ANIMAL REPRODUCTION AND ARTIFICIAL INSEMINATION, Copenhagen, Denmark, July 7-10. Prof. Ed. Sorensen, The Royal Veterinary and Agricultural College, Bülowsvej 13, Copenhagen V, Denmark.

INTERNATIONAL CONGRESS OF UROLOGY, The Waldorf-Astoria, New York, N. Y., U. S. A., Sept. 15-18. Dr. John A. Taylor, 2 East 54th St., New York, N. Y., U. S. A., Secretary-General.

INTERNATIONAL SOCIETY OF GEOGRAPHIC PATHOLOGY, Liège, Belgium, July 15-18. Dr. Fred C. Roulet, Habelstr. 24, Basel, Switzerland, Secretary General.

INTERNATIONAL UNION AGAINST TUBERCULOSIS, Rio de Janeiro, Brazil, Aug. 24-27. Prof. Etienne Bernard, 66 Blvd. St. Michel, Paris 6e, France, Secretary-General.

NEURORADIOLOGIC SYMPOSIUM, Stockholm, Sweden, Sept. 17-20. Docent Ake Lindbom, Symposium Neuroradiologicum, Serafimerlasarettet, Stockholm K., Sweden, Secretary.

PAN-AMERICAN CONGRESS OF GASTROENTEROLOGY, Mexico City, D.F., May 11-17. Dr. R. Flores-Lopez, Calle Dr. Balmis, No. 148, Mexico City, D.F., Secretary.

WORLD MEDICAL ASSOCIATION, Athens, Greece, Oct. 12-16. Dr. Louis H. Bauer, 2 East 103d St., New York 29, N. Y., Secretary General

EXAMINATIONS AND LICENSURE

NATIONAL BOARD OF MEDICAL EXAMINERS

NATIONAL BOARD OF MEDICAL EXAMINERS: *Parts I and II*, June 18-20; *Part I*, September. All centers where there are five or more candidates. Exec. Sec., Dr. John P. Hubbard, 225 S. 15th St., Philadelphia 2.

EXAMINING BOARDS IN SPECIALTIES

AMERICAN BOARD OF ANESTHESIOLOGY: Various Locations, July 18. Final date for filing application was Jan. 18. Sec., Dr. C. B. Hickcox, 80 Seymour St., Hartford 15.

AMERICAN BOARD OF DERMATOLOGY AND SYPHILOLOGY: *Oral*. Chicago, May 1952. Final date for filing application was Feb. 1, 1952. Candidates must have completed three years of approved training prior to July 1, 1952. Sec., Dr. George M. Lewis, 66 E. 66th St., New York 21.

AMERICAN BOARD OF INTERNAL MEDICINE: *Written*. Various centers and overseas, Oct. 20. Closing date for the acceptance of applications for the written examination will be May 1. *Oral*. Chicago, June 5-7, San Francisco, September or October; New York City, November or December. Subspecialty: Gastroenterology. *Examination*. Chicago, June 7. Exec. Sec.-Treas., Dr. William A. Werrell, 1 West Main Street, Madison 3.

AMERICAN BOARD OF NEUROLOGICAL SURGERY: *Oral*. Chicago, May 1952. Final date for filing applications for the May 1952 examination was Jan. 1. Sec., Dr. W. J. German, 789 Howard Ave., New Haven 4, Conn.

AMERICAN BOARD OF OBSTETRICS AND GYNECOLOGY: *Oral*. Chicago, June 7-13, 1952. Final date for filing application was Feb. 1, 1952. Sec., Dr. Robert L. Faulkner, 2105 Adelbert Road, Cleveland 6.

AMERICAN BOARD OF OPHTHALMOLOGY: *Practical*. Philadelphia, May 29-June 3; Chicago, Oct. 6-10 and New York City, June 6-10, 1953. Sec., Dr. Edwin B. Dunphy, 56 Ivie Road, Cape Cottage, Maine.

AMERICAN BOARD OF OTOLARYNGOLOGY. Toronto, May 13-17; Chicago, Oct. 6-10. Sec., Dr. Dean M. Lierle, University Hospitals, Iowa City.

AMERICAN BOARD OF PEDIATRICS: *Oral*. Washington, D. C., May 2-4; San Francisco, June 27-29; Chicago, October and Boston, late November. Exec. Sec., Dr. John McK. Mitchell, 6 Cushman Road, Rosemont, Pa.

AMERICAN BOARD OF PHYSICAL MEDICINE AND REHABILITATION: *Parts I and II*. Chicago, June 8 and 9. Sec., Dr. Robert L. Bennett, Georgia Warm Springs Foundation, Warm Springs, Ga.

AMERICAN BOARD OF PLASTIC SURGERY: *Oral and Written*. St. Louis, May 17-19. Sec., Dr. Bradford Cannon, 4647 Pershing Ave., St. Louis 8.

AMERICAN BOARD OF PROCTOLOGY. *Part I*. Kansas City, Minneapolis, Philadelphia and San Francisco, May 3. Examination includes both oral and written examinations in the basic sciences. *Dates and places tentative*. Sec., Dr. Louis A. Buie, 102-110 2d Ave., S.W., Rochester, Minn.

AMERICAN BOARD OF PSYCHIATRY AND NEUROLOGY: Chicago, June 13-14. Final date for filing applications was March 15. New York City, Dec. 15-16. Final date for filing applications is Sept. 15. Sec.-Treas., Dr. David A. Boyd, Jr., 102-110 Second Ave. S.W., Rochester, Minn.

AMERICAN BOARD OF RADIOLOGY: *Oral*. Spring 1952. Final date for filing application was Dec. 31. Sec., Dr. B. R. Kirklin, 102-110 Second Ave., S.W., Rochester, Minn.

AMERICAN BOARD OF SURGERY: *Written*. Various Centers, October 1952. Sec., Dr. J. Stewart Rodman, 225 15th St., Philadelphia.

DEATHS

Blakely, Stuart Banyar ✠ Binghamton, N. Y.; born in New York in 1882; Columbia University College of Physicians and Surgeons, New York, 1908; specialist certified by the American Board of Obstetrics and Gynecology; member of the American Association of Obstetricians, Gynecologists and Abdominal Surgeons; past president of the Binghamton Academy of Medicine and the Broome County Medical Society; fellow of the American College of Surgeons; regional consultant in obstetrics for the state department of health; as chairman of the library committee of the Broome County Medical Society, a position he held from the time of its formation in 1932 until his death, was instrumental in establishing a county medical library; a trustee of the Binghamton Public Library, and Hamilton College Library in Clinton; obstetrician, Binghamton City and Our Lady of Lourdes Memorial hospitals in Binghamton; obstetrical consultant, Tioga County General Hospital in Waverly and Ideal Hospital in Endicott; died in Binghamton City Hospital Feb. 27, aged 70, of mesenteric thrombosis.

Nalle, Brodie Crump Sr., Charlotte, N. C.; born in 1878; University of Virginia Department of Medicine, Charlottesville, 1903; at one time on the faculty of North Carolina Medical College; past president of the North Carolina Obstetrical Society and the Mecklenburg County Medical Society; fellow of the American College of Surgeons; member of the Southern Medical Association, Tri-State Medical Association of the Carolinas and Virginia and the South Atlantic Association of Obstetricians and Gynecologists; specialist certified by the American Board of Obstetrics and Gynecology; one of the founders of the Nalle Clinic, where he was chief of staff; instrumental in the building of the Memorial Hospital, where he was president, first chief of medical staff, and head of the department of obstetrics and gynecology, and where he died Feb. 13, aged 73, of coronary thrombosis.

Gerber, Isaac ✠ Pawtucket, R. I.; born in 1885; Harvard Medical School, Boston, 1910; specialist certified by the American Board of Radiology; fellow of the American College of Physicians; member of the American Roentgen Ray Society, New England Roentgen Ray Society, of which he had been president, Radiological Society of North America, American College of Radiology, and the American Radium Society; at one time vice president of the Rhode Island Medical Society; consulting radiologist at Butler, Charles V. Chapin, Miriam, Providence Lying-In, Rhode Island, and St. Joseph's hospitals in Providence, South County Hospital in Wakefield, Westerly (R. I.) Hospital, and Woonsocket (R. I.) Hospital; died in Rhode Island Hospital, Providence, Feb. 17, aged 66, of myocardial infarction.

Bell, Albert James ✠ Cincinnati; born in Cincinnati Aug. 8, 1873; Miami Medical College, Cincinnati, 1899; associate professor of pediatrics at the University of Cincinnati College of Medicine; specialist certified by the American Board of Pediatrics; member of the American Academy of Pediatrics; past president of the Cincinnati Pediatric Society; at one time chairman of the Medical Milk Commission of the Academy of Medicine; in 1941 appointed consulting pediatrician of the city health department; trustee of the Babies' Milk Fund Association; member of the staff of the Cincinnati General Hospital, where he organized and was in charge of the contagious disease department; on the staffs of Christ and Children's hospitals; died in Naples, Fla., Feb. 24, aged 78.

Wall, James Percy ✠ Jackson, Miss.; born June 25, 1878; Columbia University College of Physicians and Surgeons, New York, 1907; past president of the Mississippi State Medical Association and Central Medical Society; fellow of the American College of Surgeons; at one time vice-president of the Mississippi State Hospital Association; from 1941 to 1951 member of the House of Delegates of the American Medical Association; served during World War I; consulting surgeon, Mississippi State Tuberculosis Sanatorium in Sanatorium; member and formerly secretary of the board of trustees and attending surgeon, Mississippi Baptist Hospital, where he died Feb. 25, aged 73, of coronary thrombosis.

McCannel, Alexander J., Silverton, Ore.; born Jan. 15, 1871; Keokuk Medical College, College of Physicians and Surgeons, 1901; Georgetown University School of Medicine, Washington, D. C., 1906; member of the House of Delegates of the American Medical Association, 1921 and 1924; at one time secretary of the North Dakota State Medical Association and a member of the North Dakota State Board of Medical Examiners; fellow of the American College of Surgeons; served during World War I; formerly practiced in Minot, N. D., where he was a member of the school board; died in Silverton Hospital Feb. 5, aged 81, of uremia, following coronary disease.

Brown, Clyde Olen ✠ St. Louis; National University of Arts and Sciences Medical Department, St. Louis, 1915; assistant professor of clinical otolaryngology at St. Louis University School of Medicine; member of the American Academy of Ophthalmology and Otolaryngology; specialist certified by the American Board of Otolaryngology; affiliated with Evangelical Deaconess Hospital, Jewish Hospital, St. Luke's Hospital, St. Mary's Infirmary, and Bethesda General Hospital; died in St. Mary's Hospital Feb. 12, aged 62, of coronary thrombosis.

Armen, Garo Hovsepian, Los Angeles; George Washington University School of Medicine, Washington, D. C., 1905; assistant clinical professor of medicine at the University of Southern California School of Medicine; member of the American Medical Association and American Trudeau Society; served on the staffs of Barlow Sanatorium and California Hospital; died Feb. 6, aged 73.

Arnow, Benjamin Hilliard, Van Nuys, Calif.; Long Island College Hospital, Brooklyn, 1925; died in South Gate Feb. 6, aged 52.

Baker, Axcel Conrad ✠ Fergus Falls, Minn.; University of Minnesota College of Medicine and Surgery, Minneapolis, 1897; Northwestern University Medical School, Chicago, 1901; past president of the Northern Minnesota Medical Association; fellow of the American College of Surgeons; on the staff of the George B. Wright Memorial Hospital; died Dec. 7, aged 77, of cerebral embolism and coronary occlusion.

Barry, Shirley DeVere, Palm Desert, Calif.; Northwestern University Medical School, Chicago, 1905; member of the American Medical Association and Washington State Medical Association; died Jan. 12, aged 71.

Batchelder, Edward Carpenter ✠ Dover, N. H.; Dartmouth Medical School, Hanover, 1904; fellow of the American College of Surgeons; on the staff of the Wentworth Hospital; died Feb. 4, aged 76, of coronary thrombosis.

Billeter, William John, Bynumville, Mo.; College of Physicians and Surgeons, Keokuk, Iowa, 1887; member of the American Medical Association; served during World War I; died in La Grange Jan. 26, aged 86, of coronary thrombosis.

Blanchard, William Herbert, Assinippi, Mass.; Tufts College Medical School, Boston, 1909; fellow of the American College of Surgeons; formerly on the staffs of the Captain John Adams Hospital and Chelsea Memorial Hospital in Chelsea; served during the Mexican Border campaign and later in France during World War I; died Dec. 26, aged 64.

Boone, George H., Pottsville, Pa.; Hahnemann Medical College and Hospital of Philadelphia, 1894; died in Warne Hospital Feb. 12, aged 80.

Brookshire, Harley Gaskill Sr., Asheville, N. C.; North Carolina Medical College, Davidson, 1905; served as a director of the Aston Park Hospital; died Feb. 7, aged 73.

✠ Indicates Fellow of the American Medical Association.

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Brown, John Robert ✠ Los Angeles; Western Pennsylvania Medical College, Pittsburgh, 1899; an Associate Fellow of the American Medical Association; formerly practiced in Pittsburgh, where he was affiliated with the Passavant and Southside hospitals and was chief surgeon for the Wabash Railroad; from 1925 to 1951 surgeon for the Hollywood Presbyterian Hospital; died Dec. 27, aged 83.

Buckley, Ralph Emerson ✠ Conyngham Pass, Pa.; Medico-Chirurgical College of Philadelphia, 1904; an Associate Fellow of the American Medical Association; served in France during World War I and was awarded the Purple Heart; formerly practiced in Hazleton, where he was a member of the board of trustees of the Hazleton State Hospital and president and a member of the board of directors of the Chamber of Commerce; died in St. Joseph Hospital, Hazleton, Feb. 11, aged 69.

Burke, William Patrick, Los Angeles; College of Physicians and Surgeons of Chicago, 1894; died Feb. 16, aged 82.

Burnham, Clark James, Berkeley, Calif.; University of California Medical School, San Francisco, 1891; an Associate Fellow of the American Medical Association; died Feb. 15, aged 83.

Butz, Alfred S., Philadelphia; University of Pennsylvania Department of Medicine, Philadelphia, 1893; also a graduate in pharmacy; died Feb. 11, aged 86.

Caldwell, Spencer Burnham ✠ Baldwin, N. Y.; University of Vermont College of Medicine, Burlington, 1921; served during World War I; affiliated with Mercy and South Nassau Communities hospitals in Rockville Centre; died Feb. 9, aged 54, of coronary disease.

Casper, Joseph Francis, Jasper, Ind.; University of Louisville (Ky.) School of Medicine, 1910; served during World War I; affiliated with Dubois County Memorial Hospital, where he died Jan. 18, aged 63, of cerebral hemorrhage.

Chapin, Anna Dewey, Los Angeles; the Hahnemann Medical College and Hospital, Chicago, 1902; died Jan. 31, aged 80.

Clements, Henry W., Adel, Ga.; University of Georgia Medical Department, Augusta, 1900; member of the American Medical Association; affiliated with Memorial Hospital, where he died Feb. 6, aged 74.

Crecelius, William Anton, Sandusky, Ohio; Cleveland Homeopathic Medical College, 1898; affiliated with Providence and Good Samaritan hospitals; died Jan. 17, aged 85, of cardiovascular renal disease.

Crum, Edwin Wallace, Waverly, Ill.; Barnes Medical College, St. Louis, 1900; member of the American Medical Association; affiliated with Passavant Memorial and Our Saviour's hospitals in Jacksonville; died in St. Petersburg, Fla., Feb. 13, aged 75, of coronary thrombosis.

Crumpton, Joseph W., Starkville, Miss.; University of Tennessee Medical Department, Nashville, 1883; served on the state board of health and the state house of representatives; twice elected to the state senate; died Feb. 20, aged 92.

Daily, Louis ✠ Houston, Texas; University of Texas School of Medicine, Galveston, 1910; professor of clinical otolaryngology at the Baylor University College of Medicine; specialist certified by the American Board of Otolaryngology; member of the American Academy of Ophthalmology and Otolaryngology; fellow of the American College of Surgeons; affiliated with Jefferson Davis, Memorial, and Methodist hospitals; died Jan. 29, aged 69, of coronary thrombosis.

Dallas, William Buel, Jefferson City, Mo.; St. Louis College of Physicians and Surgeons, 1923; died Nov. 30, aged 61, of coronary occlusion.

Dancy, Henry Hyman, Phoenixville, Pa.; University of Pennsylvania Department of Medicine, Philadelphia, 1902; also a pharmacist; died Dec. 18, aged 79.

Daniel, Walter Wright ✠ Atlanta, Ga.; Emory University School of Medicine, 1923; past president of the Fulton County Medical Society; fellow of the International College of Surgeons; member of the American Academy of General Practice and one of the founders and past president of the Georgia chapter; served overseas during World War I; formerly on the faculty of his alma mater; affiliated with Crawford W. Long Memorial Hospital; died Feb. 24, aged 55, of thrombosis and infarction of the cerebellum.

DeLorme, Homer Arthur, St. Louis; Louisville (Ky.) Medical College, 1892; died Jan. 24, aged 83, of hypertensive heart disease.

Dickson, George Bennett ✠ Shreveport, La.; Medical Department of Tulane University of Louisiana, New Orleans, 1911; formerly Caddo parish deputy coroner; served during World War I; for many years affiliated with North Louisiana Sanitarium; died Feb. 2, aged 64, of a heart attack.

Dixon, Herbert Sidney, Brooklyn; College of Physicians and Surgeons, medical department of Columbia College, New York, 1892; died Feb. 17, aged 86.

Donnelly, John Devlin ✠ Bala-Cynwyd, Pa.; University of Pennsylvania School of Medicine, Philadelphia, 1914; specialist certified by the American Board of Pediatrics; past president of the Philadelphia Pediatric Society; served overseas during World War I; affiliated with Misericordia Hospital in Philadelphia and Bryn Mawr (Pa.) Hospital where he died Feb. 9, aged 61, of coronary occlusion.

Eisaman, Cecil LeRoy, Marion, Ind.; Indiana University School of Medicine, Indianapolis, 1925; member of the American Medical Association; served during World War I; died Feb. 10, aged 52.

Elliot, Francis Theodore, Hagerstown, Md.; Jefferson Medical College of Philadelphia, 1911; also a graduate in pharmacy; died Feb. 11, aged 68, of coronary occlusion.

Fleming, John Carl ✠ Dallas, Pa.; Medico-Chirurgical College of Philadelphia, 1908; specialist certified by the American Board of Otolaryngology; on the staff of the Nesbitt Memorial Hospital in Kingston; died in Methodist Hospital, Philadelphia, Feb. 11, aged 68, of coronary thrombosis.

Fox, Warren Franklin, San Bernardino, Calif.; College of Physicians and Surgeons, Los Angeles, 1913; member of the American Public Health Association; formerly city health officer; died Feb. 19, aged 61.

Gaver, Earl Elbert, Orient, Ohio; Ohio Medical University, Columbus, 1902; veteran of the Spanish-American War and World War I; affiliated with Orient State School, where he died Feb. 24, aged 76, of coronary occlusion.

Gessner, Francis Emil ✠ Dallas, Texas; Yale University School of Medicine, New Haven, 1912; member of the American Academy of General Practice; for many years member of the city-county welfare board; served during World War I; on the staff of Methodist Hospital; died Feb. 4, aged 61, of a heart attack.

Gilbert, Bernard Horace, San Jose, Calif.; University of Vermont College of Medicine, Burlington, 1913; member of the American Medical Association; died in San Francisco Jan. 23, aged 65, of ruptured abdominal aneurysm.

Gingold, Joseph Randolph ✠ Meadville, Pa.; Syracuse University College of Medicine, 1923; specialist certified by the American Board of Radiology; member of the Radiological Society of North America and the American College of Radiology; on the staff of Spencer Hospital, where he died Feb. 2, aged 52, of multiple myeloma.

Girsdansky, Joseph, New York; University and Bellevue Hospital Medical College, New York, 1911; member of the American Medical Association; served during World Wars I and II; formerly on the staff of Gouverneur Hospital; died on vacation in Boothbay Harbor, Me., Feb. 14, aged 61, of cerebral hemorrhage.

Goldenberg, Theodore, Buffalo; Hessische Ludwigs-Universität Medizinische Fakultät, Giessen, Hesse, Germany, 1903; member of the American Medical Association; on the staffs of the Millard Fillmore and Lafayette General hospitals; died Feb. 16, aged 71.

GOVERNMENT SERVICES

ARMY

General Raymond A. Kelser Is Dead.—Brig. Gen. Raymond A. Kelser, retired, former chief of the Army Veterinary Corps, died April 16 at his home in Philadelphia, aged 59. General Kelser was a widely known bacteriologist and immunologist. He was commissioned a first lieutenant in the Army Veterinary Corps in 1918, was director of the first army veterinary laboratory at Letterman General Hospital, San Francisco, and for many years commanded the veterinary laboratory section of the Army Medical School in Washington, D. C. During this latter period he was instructor in bacteriology and infectious diseases at the Army Veterinary School and the American University. He was a fellow in bacteriology at Harvard University Medical School in 1933, and later he was a member of the Army Medical Research Board in the Canal Zone. While serving on the Medical Research Board in the Philippines, he developed an improved vaccine that enabled the Philippine Government to erradicate rinderpest from those islands. In 1932 and 1933 he conducted experiments that proved that equine encephalomyelitis, a disease that had killed large numbers of horses in this country, was transmitted by mosquitoes. General Kelser was chairman of the American delegation on the Joint American-Canadian Commission on Rinderpest during World War II. He was appointed chief of the Army Veterinary Corps in 1938, and served in that capacity throughout the war. He was awarded a Ph.D. in 1923 by the American University in Washington, the International Veterinary Congress Prize by the American Veterinary Association, and the degree of Honorary Associate of the Royal College of Veterinary Surgeons in London, and the Army Distinguished Service Medal. General Kelser was buried with full military honors in Arlington National Cemetery in Washington.

Call 265 Reservists to Active Duty.—Two hundred and sixty-five officers of the Army Medical Service Reserve will be ordered into active military service in July, the Department of the Army announced April 11. This is in addition to the original call for 290 officers made in March. Included in the new group are 232 physicians, 25 dentists, and 8 veterinarians. Quotas have been assigned to each of the six Army areas in the continental United States, as well as U. S. Army, Pacific, and U. S. Army Caribbean.

Under the law, priority 1 registrants are defined as those educated at government expense and others deferred from service to pursue a medical or dental education, who spent less than 90 days on active service in World War II following their training. Priority 2 registrants differ only in that they have spent more than 90 days but less than 21 months on active service in World War II following their training. However, the Army is selecting those with the least amount of creditable service first and no one with more than 12 months of previous service will be called. Physicians and veterinarians will continue to be selected entirely from the volunteer reserve, classified as priority 1, but dentists with priority 2 rating will be called. Medical officers selected will be ordered into the active military service for a maximum period of two years.

Preventive Medicine Conference.—Experts of the Army Medical Service and civilian authorities held a 10 day conference in April in Washington on preventive medicine. Representatives of the medical departments of the Navy and Air Force and the chief preventive medicine officer of each Army area in this country and others from Army installations and post hospitals attended. Sessions were conducted in the graduate school at Walter Reed Army Medical Center and included a two day field trip to Camp Detrick, Md. Papers were presented by faculty members of the graduate school and the medical field service school at Fort Sam Houston, Texas, by the preventive medicine division in the Army Surgeon General's Office and by civilian specialists. Sessions were devoted also to atomic and biological warfare, communicable diseases, immunology, chemotherapy, industrial medicine, environmental control and health education, safety, and training.

MISCELLANEOUS

Institute of Civil Aviation Medicine Proposed.—The establishment of an Institute of Civil Aviation Medicine is now a major objective of the Aero Medical Association, it has been announced by Dr. W. R. Stovall, recently installed president. Dr. Stovall, who is chief of the medical division, Office of Aviation Safety, Civil Aeronautics Administration, cites five functions such an institute might perform:

1. It would serve as a focal point for civilian aviation medical activities, containing laboratories for carrying out projects that could not more economically be conducted at universities or other medical laboratories. 2. It would have facilities for resident training of medical examiners to obtain a better understanding of the pilot and his physical demands, and for conducting preliminary extension training courses for physicians who could not conveniently leave their practices for an extended period. 3. It would make possible better field instruction of CAA medical examiners. 4. It would contribute to aviation safety by applying preventive medicine techniques to those human factors which root in physical difficulties. 5. It would concentrate civilian aviation medical needs and activities in a proper atmosphere, permitting studies on civilian aviation medical problems that are not covered by military research and development.

Public concern for every aspect of aviation safety, and the relation of civil aviation problems to the needs of national defense underline the importance of establishing such an institute, Dr. Stovall said. He suggested establishment of the institute at a convenient place such as Indianapolis or Oklahoma City, or at a university that might be able to make its facilities available. The institute would work with outside organizations that are carrying out research contracts on civil aviation medicine.

Dr. Stovall pointed out that the American Advisory Board on Medical Specialties and the American Medical Association's Council on Medical Education and Hospitals delayed granting specialty status to aviation medicine because of the lack of educational and training facilities for civil aviation medical examiners, industrial civil aviation physicians, and other civil flight surgeons.

Number One Killer at Bituminous Coal Mines.—Fifty per cent of all fatalities that occurred underground at bituminous coal and lignite mines in 1951 resulted from falls of roof, face or rib, according to a Bureau of Mines report. The bureau's study reveals that human failure was responsible for 80% of the fatalities and unforeseeable dangers and unavoidable risks for 20%.

Management failure was responsible for 50% of the human-failure fatalities, employee failure accounted for 23%, and joint or undetermined human failure for 7%. However, "Many managers," the report states, "have made such determined efforts toward eliminating the roof-fall menace that their mines have been operated for long periods of time without a fatality. Also, many miners have treated the mine roof with a respect that has allowed them to work 30, 40 or even 50 years without being injured." The average dimensions of the pieces of roof-rock that fell and caused fatalities were 13 ft. long, 10 ft. wide and 1 ft. in maximum thickness. The comparatively large area of these falls emphasized the great need for better roof control standards and strict compliance therewith by both officials and workmen.

Forty-eight per cent of the fatalities occurred in places where coal was loaded mechanically, and the remaining 52% occurred in hand-loading places. Forty (14%) of the 292 fatalities occurred while the foremen were in the places where the falls occurred; they include those cases where the foreman was a victim. In numerous other instances, the fall occurred within minutes after the foreman had visited the place. This indicates that some foremen are unaware of all unsafe conditions or measures that should be taken, or they place production ahead of safety. The report contains recommendations designed to reduce the number of roof-fall fatalities. A free copy of HHS 406, "Falls of Roof The No. 1 Killer at Bituminous Coal Mines 1951," by T. L. Back and H. F. Weaver, can be obtained from the Bureau of Mines, 4800 Forbes St., Pittsburgh 13.

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FOREIGN LETTERS

DENMARK

Private Practitioner or Government Specialist?—In a lecture delivered to the Irish Academy of Medicine in November, 1951, Dr. Johannes Frandsen, director-general of the Danish Health Service, traced the evolution of this service during the last few years and drew attention to the difficulties encountered in coordinating health activities. A new medical field has been created in the last 10 years, and it was suggested that an activity such as wholesale diphtheria immunization could be more cheaply and, perhaps, more effectively carried out by young physicians and nurses than by general practitioners. It was also suggested that pediatricians be appointed to examine children. But Dr. Frandsen had no doubt that the newly created medical work belonged by right to the general practitioner and that it was imperative to use his knowledge and energy in any public health service. "If you push him aside and deprive him not only of the work but also of the chance of earning something, first in one field and then in another, the result will be a disillusioned hard-up profession; and an impecunious doctor who has lost courage and who cannot afford to keep his medical knowledge abreast of the times is apt to be both dangerous and costly to society."

Turning to the special field of tuberculosis, Dr. Frandsen pointed out the need for adapting antituberculosis measures to the special needs and conditions of different countries. It cannot be assumed that "the fight against tuberculosis can be conducted according to one universal, international plan." In each county in Denmark there is now a dispensary system with a tuberculosis hospital at the center, its director being in charge of both hospital and dispensary. Half of the cost of the dispensaries is refunded by the state. Tuberculosis is diminishing so rapidly in Denmark that some tuberculosis institutions may soon have to be diverted to other uses. The dispensaries will, however, continue to function for a long time to come, and the maintenance of BCG immunization, now general throughout the country, will be assured. Both BCG and diphtheria immunization are provided free of charge. In 1950, there were only 14 deaths per 100,000 persons from all forms of tuberculosis, a remarkable fall from 78 per 100,000 deaths in 1927. Denmark's freedom from bovine tuberculosis at the present time is largely to be credited to the Federation of Danish Dairy Organizations.

Dr. Frandsen's account of the Danish hospital system emphasized the importance of the part played by the private general practitioner. There are now 10.4 hospital beds of every description per 1,000 inhabitants. Each county has at least one large central hospital as well as several smaller hospitals, each with 50 to 100 beds in the charge of a surgeon. "If we are to improve our hospital system and keep it abreast of medical progress, it is essential for financial reasons to take care that the hospitals do not grow bigger and treat more patients than is necessary." To this end efforts are made to provide the almost 2,500 well-trained general practitioners with facilities for laboratory tests and specialist examinations, so that as many patients as possible can be treated at home. Most of the central hospitals are now equipped with laboratories in which investigations can be undertaken on behalf of general practitioners.

Dr. Frandsen also referred to the successful experiment carried out with the help of the Rockefeller Foundation in combatting a comparatively high infant mortality. During this 6-year experiment nurses visited homes and taught mothers how to care for their children during the first year of life. This experiment was carried out in two rural districts and in a Copenhagen slum. The infant mortality in the selected districts was halved. An act extending this work was quickly passed and became a turning point in Danish health legislation, for it was the first law aimed at preserving the health of healthy persons. More than half of the children in Denmark are now under the regular supervision of a health nurse. Since 1945, preventive health legislation has been extended to expectant mothers, who now have the right during pregnancy to be examined three times by a doctor and seven times by a midwife. These and many other free examinations are offered to children from birth onwards, regardless of their social standing.

ACTH and Cortisone for Diseases of the Eyes.—At a recent meeting of the Ophthalmological Society in Copenhagen, Dr. Elise Vesterdal gave an account of the treatment with corticotropin (ACTH) or cortisone of 111 patients suffering from diseases of the eyes. This treatment was started in June, 1950, and since then considerable experience with it has been acquired at the eye department of the Rigshospital, where 45 patients have been given inpatient treatment. Most of the other patients were ambulatory cases treated at the Eye Polyclinic. In 52 cases only corticotropin treatment was given and in 33 cases only cortisone, while in 26 cases both preparations were given either simultaneously or consecutively. In every case the observation period lasted more than two months.

The opinion Dr. Vesterdal has formed of the value of this treatment is guarded, yet at the same time most favorable. During observation periods ranging from 3 to 15 years she found that cortisone given locally was highly effective in various diseases of the eye, including allergic conjunctivitis with palpebral eczema, nodular episcleritis, sclerokeratitis, acne rosacea keratitis, parenchymatous keratitis (metaherpetic as well as syphilitic), and mild cases of acute iritis. In some cases of inflammation of the posterior segment of the eye, such as iridocyclitis, treatment with corticotropin was dramatically effective. No significant or permanent ill-effects were observed after the parenteral administration of corticotropin, and the local administration of cortisone did not produce any side-effects whatever. Even though it may seem that the action of these preparations is merely symptomatic, without the radical removal of the original causal factors and without any guarantee against ultimate relapse, it has so many advantages over other methods of treatment that its adoption in ophthalmology is fully justified as a matter of everyday practice in conjunction with more directly causal therapeutic measures. Indeed, it may be said that at the present time the greatest enthusiasm exists with regard to the purely therapeutic effects of corticotropin and cortisone in ophthalmology. Among the many reasons for this enthusiasm is the comparative cheapness with which these expensive preparations can be given in ophthalmologic practice. Another great advantage is the absence of those complicating ill-effects, which these preparations have provoked when given in comparatively large doses for diseases in other parts of the body.

MEXICO

Reorganization of Mexico City General Hospital.—In 1905, Mexico City, with a population of 500,000, dedicated the municipal general hospital, which had a capacity of 1,000 beds. The General Hospital of Mexico City soon became the most important clinical institution in the country and one of the best in Latin America. The school of medicine taught most of the different services, and its staff included members of international prestige: Dr. Fernando López, Dr. José Terrés, Dr. Angel Gaviño, and Dr. Genaro Escalona, among others. The cardiology department, of which Prof. Ignacio Chavez was the head, included most of the investigators who later became chiefs and senior members of the departments of the Instituto Nacional de Cardiología, when this institution was founded in 1944. The department of internal medicine constituted the nucleus on which the Hospital de Enfermedades de la Nutricion was created in 1946.

But by the late thirties it was clear that the capacity of the general hospital was inadequate to accommodate the growing population of Mexico City (3,000,000 in 1950) and that the distribution of its services and departments, in more than 50

The items in these letters are contributed by regular correspondents in the various foreign countries.

separate buildings, was not functional. Such problems became acute in the last years, during which the medical and nosocomial standards of the institution were not as high as they had been. Nevertheless, until Mexico City builds a new modern general hospital, the present institution is indispensable. With several excellent services and departments still functioning, some months ago the medical staff began to study and act on plans for a temporary reorganization. Dr. Mariano Vázquez, chief of one of the surgical services for more than 20 years, was chosen medical director last January. Owing to his personal qualities, the cooperation of the medical staff, and financial help from the federal government, it is expected that a substantial improvement will take place at the general hospital. Meanwhile, a better institution is being planned.

Anniversary of Professor Cosío-Villegas.—In Mexico, where there are still around 300,000 patients with tuberculosis, phthisiology is a specialty of considerable importance. Prof. Ismael Cosío-Villegas has been responsible in great part for the development of this branch of medicine in this country.

In 1929, with the advice of Professor Gea-González and at the request of the federal sanitary authorities, he planned the Campaña Nacional contra la Tuberculosis (National Campaign Against Tuberculosis), a vast and accomplished organization. Professor Cosío-Villegas has been chief not only on that occasion but again in 1938 and in 1945. It was in that capacity that he created the first tuberculosis hospitals and dispensaries, and in order to provide medical staffs for them he organized, for the first time, postgraduate studies in phthisiology, which have continued to be given every year since. Now there are four tuberculosis hospitals (average capacity: 600 beds), two in Mexico City, one near the Gulf of Mexico, and the other in Guadalajara, which is the second largest city of the country. A brilliant expositor, Professor Cosío-Villegas has occupied one of the chairs of clinical medicine at the school of medicine and has participated in numerous scientific meetings, national and foreign; he was chairman of the Eighth Pan-American Congress of Phthisiology, which was held in January, 1949. He has written more than 100 papers and communications and is the author of an excellent textbook of pneumology.

Last January, on the occasion of the 25th professional anniversary of Professor Cosío-Villegas, several events took place to honor him. There were three medical meetings, during which 48 papers were read and commented on by Professor Cosío-Villegas' friends, pupils, and collaborators, and which made an appraisal of the present status of Mexican phthisiology. All of them will be included in a commemorative volume, which will be published this year.

PARIS

New Treatment of Leprosy.—Professor Gaté (Lyons) reported the preliminary results of treating leprosy with bi-dihydrochaulmoogroyl-4,4' diamino-diphenyl-sulfone, a combination of chaulmoogra oil and diamino-diphenyl-sulfone (D. D. S.) radicals. The drug was developed by M. Chambon, professor of organic chemistry and toxicology (Lyons), who previously prepared delactonized and selectively hydrogenized chaulmoogra oil, whose low toxicity and intramuscular and intradermic diffusibility has permitted, since 1949, prolonged treatment with large doses, at the Lyons leprosary. Diamino-diphenyl-sulfone has an unquestionably beneficial effect on leprosy, but it is poorly tolerated by aged patients.

It is used as a 5% suspension. Each series of injections consists of 2 deep intramuscular injections of 10 cc. per week for a total of 20 injections, 15 days intervening between each series. Preliminary trials on 17 patients from 10 to 73 years of age resulted in clinical improvement of all types of leprosy. Leprids were always favorably influenced early; after attentuation of their color and progressive diminution of their size, the skin resumed its normal appearance or retained only a yellowish or light brown pigmentation. Moreover, lepromas disappeared rapidly; in a 70-year-old woman, whose lepromas did not totally disappear after oral administration of sulfones and who tolerated diamino-diphenyl-sulfone badly, the new remedy brought about complete deflation of the lepromas, together with clearing of the pigmented spots, under which there was no more infiltration. In a case of ulcerous leprosy, lepromas of the face disappeared before the conclusion of the first series of injections; after the sixth injection, the cicatrising of ulceration was already in progress. Moreover, two patients with ocular lesions with iritis, one with free lepromas in the vitreous humor and the other with corneal lepromas, could be treated without the undesirable sulfones. In nerve lesions, the alleviation of pain and the diminution of the hypertrophy of the nervous trunks as well as arrest of atrophy occurred rapidly. Histological results are encouraging; along with the reduction of Hansen's bacilli, which often became granular, a lymphocytic reaction and a modification of infiltration were noted. Local and general tolerances were excellent, even in the patient who tolerated orally administered sulfones poorly. There were no contraindications because of age, general condition, or coexisting disease.

Severe Shock by Vitamin B_1.—Benmussa and Diacono (Tunis) have just reported a severe case of true shock with collapse occurring in a 57-year-old physician who received a daily injection of 100 mg. of thiamine hydrochloride for sciatic neuralgia. The first four injections were well tolerated; three minutes after the fifth injection, he experienced malaise, screamed, vomited, and collapsed. A few moments later, examination revealed the complete abolition of all reflexes, a comatose appearance, intensive congestion, with cyanosis, loss of consciousness, abolition of radical pulse, heart sounds that were barely perceptible because of noisy respiration, and a lowering of the arterial blood pressure. The patient remained in this condition during the entire night, during which two intestinal hemorrhages occurred, one hour apart. Ten hours after the onset of the accident, a hemogram was performed, which revealed marked hemoconcentration. In order to relieve the shock, a massive transfusion, by perfusion, of 500 cc. of diluted blood, at the rate of 140 to 160 drops per minute, was instituted, and this was alternated with 500 cc. of polyvinyl-pyrrolidone "subtosan." After injection of a liter of fluid, improvement was spectacular; the pulse became intermittently perceptible; and after 1,500 cc. of total fluid was administered the heart was beating regularly (88 beats per minute). After 1,700 cc. was administerd (1,000 cc. of diluted blood and 700 cc. of polyvinyl-pyrrolidone), transfusion was discontinued. After a quiet night, improvement progressed rapidly; on the following day the patient felt normal and was euphoric. He resumed his activities after a rest of five days.

***p*-Aminosalicylic Acid in Pulmonary Tuberculosis.**—In order to obtain an adequate blood level of *p*-aminosalicylic acid (PAS) over an extended period, large doses must be given orally, but this can rarely be done, because of the appearance of digestive disorders. Intravenous administration gives adequate levels, but the rapid elimination of the drug necessitates continuous perfusion. A pure, pyrogen-free solute of *p*-aminosalicylic acid has been developed and used for over a year by Paraf and Zivy and their associates in the pharmacy laboratory of the Bichat Hospital. A quantity of 500 cc. of this solution, containing 15 gm. of *p*-aminosalicylic acid, is perfused by drip for two and a half to three hours. The blood concentration shows high peaks, which favors passage of the drug through the fibrous and vascular barriers; perfusions may be administered for one or two months without inconvenience. Results are interesting, especially in patients with cavitary tuberculosis, in whom streptomycin and *p*-aminosalicylic acid administered orally are ineffective. Of the 40 patients treated, there was noticeable improvement in 88%. The field of collapsotherapy was widened, a pneumothorax often being made possible by the perfusions. In 10 to 15% of the patients, perfusions of *p*-aminosalicylic acid seem to be ineffective, but combination with streptomycin reduces the number of failures. The authors also stressed that these perfusions with streptomycin resulted in 42 patients with cases of recent acute meningitis, in complete recovery in 76.2%. This recovery, which has lasted 18 months thus far, has permitted the resumption of scholastic and professional activities. Even in 21 patients with long-standing cases, when streptomycin was insufficient or had become ineffective, perfusion of *p*-aminosalicylic acid resulted in complete recovery in 5 patients (which has now lasted 18 months); 5 patients are in good condition; 3 have not done well, and 9 have died. Recently, Paraf reported that when intravenous perfusions in children are not possible, subcutaneous perfusion may be performed.

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Treatment of Lipoid Nephrosis with ACTH.—On Nov. 23, 1951, at a meeting of the Medical Society of the Paris Hospitals, Professor Debré and Drs. P. Mozziconacci, Attal, and Caramanian discussed results of corticotropin therapy in 17 cases of pure lipoid nephrosis, without nephritis, important azotemia, or noticeable hypertension, which constitute a contraindication for this treatment. The 17 cases treated resulted in four complete successes, nine partial successes, and four failures. They gave from 50 to 75 mg. of corticotropin daily for 8 to 10 days. Forty-eight hours after completion of the treatment, an outbreak of diuresis of 2 to 3 liters occurred, which lasted 24 hours and was followed by a rapid "melting away" of edema. If this outbreak occurs during the course of the treatment, treatment may be interrupted immediately. The effect on the blood syndrome is less certain. Professor Debré and his co-workers emphasized that corticotropin does not constitute a specific treatment of lipoid nephrosis, and also that there is not sufficient time elapsed to determine in what degree its effect on the edema contributes to the cure of the disease. They noted the total failure of cortisone in the treatment of lipoid nephrosis. They also frequently observed that dehydration occurred during treatment. In such cases they recommend the discontinuation of the salt-free diet after cessation of corticotropin and resumption of a low chloride diet. They stressed at the same time the necessity of a strictly salt-free diet during corticotropin treatment in order to avoid acute edematous accidents. Several other authors (Prof. Julien Marie in 10 cases, Azerard in 2, Derot in 2, and Clement in 2) noted the same results. Professor Marie stated that one relapse occurred during the months following the treatment.

SPAIN

Congress of Surgery.—The Third International Congress of Surgery will take place in Madrid from May 19 to May 24. The following subjects will be discussed: (1) surgery of vesical tumors, by Professors R. Darget (Burdeos), Boeminghaus (Duesseldorf), Gil Vernet (Barcelona), O. S. Lowsley (New York), R. Freitas (Sao Paulo), and Oheeron (Texas); (2) hip surgery, by Professors Brittain (Norwich), Judet (Paris), Rodriguez de Mata (Madrid), R. Anderson (Washington), E. Compere (Chicago), and Montagne (Lima); and (3) cardiovascular surgery, by Professors Valdoni (Rome), Derra (Duesseldorf), Piulachs (Barcelona), Taiana (Buenos Aires), Bailey (Philadelphia), and A. Ochsner (New Orleans).

The organization committee of the congress is headed by Prof. Martin Lagos (faculty of medicine of Madrid), and the vice-presidents are Professors Garcia Orcoyen (dean of the faculty of medicine of Madrid), A. De La Peña (professor of urology of the faculty of medicine of Madrid), and J. Soler Roig (Barcelona). The secretary general of the congress is Professor A. De La Fuente (professor of surgery of the faculty of medicine of Madrid). The presiding officer of the section on communications is Dr. M. Merchan (assistant professor of surgery of the faculty of medicine of Madrid).

Inquiries should be addressed to the Instituto Nacional de Medicina y Seguridad del Trabajo, Facultad de Medicina, Pabellón Núm. 8, Ciudad Universitaria, Madrid, in the name of the secretary general of the congress mentioned above.

SWITZERLAND

Danger to Freedom of Practice of Medicine.—There has been in Switzerland, since 1911, a law regarding insurance against illness and accident; this law is supposed to protect the poor who must be members of a mutual benefit society. For many years, since only poor persons were members of the sick-fund, the Swiss physicians charged a low rate ($0.75) for consultation, in spite of the increased cost of living. In the German part of Switzerland, the sick-funds became increasingly powerful and obliged all physicians to sign agreements with them. Then, little by little, middle class and wealthy persons were accepted in the sick-fund and could have the benefit of treatments at the same rate as the poorer persons. The physicians of the French part of Switzerland always refused to sign such arrangements with the sick-funds; they compromised, and the physician would charge his patient according to his economic status. The patient could obtain from the sick-fund the repayment of $0.75, paying the difference to the practitioner. This modus vivendi was criticized by the sick-funds, which reasoned that when the patients regularly pay their assessment to the sick-fund they should be treated according to the law on insurance against illness and accidents, which guarantees them the application by the physician of the maximum rate. Two arguments can be opposed to this opinion and cancel it. The law, dating from 1911, was made only for persons of low financial condition in order to assure them of treatments at a low price, while, in 1948, 65% of the Swiss population were members of sick-funds. Chiefly, the rates that were suitable in 1911 are far too low at the present time.

The Swiss government, stimulated by the sick-funds, which wield political power, made an arbitrary decision on July 20, 1951, which obliged the physician to treat all members of the sick-funds at the maximum rates ordered by the law. If the patient agreed to pay more than the maximum rate in order to help the physician defray the increased cost of living, the sick-fund is not allowed to repay him the amount that he is supposed to receive according to his right. Thus, the physician can either refuse to treat the insured persons (this if still possible according to the law) or to treat them, but only at the rate of the sick-fund. The insured is injured too; this governmental decree is a hindrance to his liberty in choosing his physician, for he is obliged to consult only practitioners who have signed the agreement with the sick-funds; he cannot thus have the attendance of specialists who refuse to accept the maximum rates, unless they themselves pay the whole amount of the consultation. The Federation of the Swiss Physicians made an energetic protest against this decree at an extraordinary general meeting last summer.

Just after this decree, much criticized also by the Swiss Society of Jurists, was issued, a second one, even more arbitrary, was formulated by the ministry of public economy of Switzerland toward the physicians of Geneva. These practitioners, although they had not signed any agreement with the sick-funds, are obliged to accept a fee of $1.00 for a consultation and of $1.33 for a visit at the house of the patient; this decree was taken on the advice of the "Office fédéral de contrôle des prix," which is supposed to fight against the increased cost of living. These fees were based on those charged by physicians of Geneva before 1939 for the members of sick-funds who were poor; thus a fee that was minimal in 1939 would be maximal for 1952.

Swiss physicians insist on the division of the persons insured in different categories: (1) the poor class with legal minimum scale of price; (2) persons with average incomes for whom the legal maximum scale will be charged without being exceeded, and (3) wealthy persons with free scales of price, who can obtain a repayment of a part of the fees they pay to the physician. This seems to be the only way of compromising with the sick-funds.

There is another problem facing the patients. The "Concordat des caisses-maladie" of Switzerland established, about 20 years ago, an official list of pharmaceutical products, which are the only ones that can be prescribed to the insured persons of sick-funds; every 2 or 3 years, this list is renewed in order to follow the progress of therapeutics. This list is approved by a commission of medical experts who do not have enough time to thoroughly study the propositions made by the direction of the sick-funds. It becomes obligatory for the physician to prescribe a remedy from the list; otherwise it is the patient who has to pay for it. Since only persons without medical information deal with the applications of the list, it has often happened that urgent treatments with penicillin, streptomycin, or chloramphenicol could not be fulfilled because the sick-fund did not accept it. The list in question is set without any scientific criterion, and the directors of different pharmaceutical firms have made protestations against it, for their products, though excellent, were not accepted for this list, not having had the agreement of the heads of the sick-funds. The patients suffer very much from this, as they cannot have the benefit of some efficient therapeutics unless they pay for it themselves; the physicians are wronged in that they cannnot prescribe the treatment they would judge the most judicious.

CORRESPONDENCE

POLLEN PREVALENCE AND POLLEN-FREE AREAS

To the Editor:—I have read with interest the article entitled "Pollen Prevalence and Pollen-Free Areas" by Orin C. Durham, which appeared in THE JOURNAL (**148**:716 [March 1] 1952). Mr. Durham's approach to the pollen problem may perpetuate a fallacy in the mind of the average physician reader. There is an implication first, that it is possible to escape a pollen allergy and second, that there are certain areas, suggested by the accompanying maps, to which a pollen sensitive person may flee.

In the first instance, a basic tenet of the field of allergy states that it is the predisposition to become sensitized rather than the sensitizing agent that controls the fate of the allergic person. Experience in Southern California demonstrates this with monotonous regularity. A person sensitive to eastern pollen who moves to this area will probably become sensitized to our local flora within a period of from 6 to 18 months. This new sensitivity is as strong and the symptoms often as intense as they were when the person lived in the East. Some of these persons moved here because of the type of advice that Mr. Durham's article suggests.

I do not wish to criticize Mr. Durham's excellent observations. He properly offers no clinical advice, but I believe that the article almost demands that the reader draw conclusions that are frequently erroneous and can lead to considerable economic and social dislocation for those who heed such advice, pack up their worldly goods and head for the pollen-free open spaces where ragweed is no more. Unless such articles as this are confined to specialized journals or guarded by proper caution to the overzealous reader, both article and author become the victims of unfortunate misinterpretation. Author, reader, and patient are the losers thereby.

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ANTABUSE®-ALCOHOL REACTION FOLLOWING USE OF AFTER-SHAVE LOTION

To the Editor:—In October, 1951, tetraethylthiuramdisulfide (antabuse®) was approved for sale on physicians' prescription as a useful adjunct in the treatment of alcoholism. Prior to this time, controlled investigations of the drug were made in the United States and Canada in selected clinics and institutions. Since it is anticipated that the drug will be widely used, the following experiences are reported as indicative of some of the cautions that must be exercised in treating patients with this drug.

Two hospitalized patients were started simultaneously on tetraethylthiuramdisulfide therapy after the usual precautions concerning evaluation of cardiac and liver function. The dosage given was 0.5 gm. daily for two weeks. At the end of this period the patients were given 15 cc. of 100-proof whiskey by mouth, which was swallowed rapidly. Fifteen minutes later, patients were permitted to sip another 15 cc. of 100-proof whiskey. In each case, with the second drink of whiskey, the anticipated reaction of flushing of the face, scleral injection, tachycardia, sense of constriction of the throat, and nausea were observed. After this initial conditioning test, both patients were given a reduced dose of 0.25 gm. of the drug daily. On the second day of reduced dosage, each patient applied an after-shave lotion, containing approximately 50% alcohol, to the face after shaving. Within five minutes, both patients experienced warmth and flushing of the face, with areas of blotching, waves of nausea, and the typical apprehension of a mild tetraethylthiuramdisulfide-alcohol reaction. Although the reaction was not severe, it was more dramatic than the controlled alcohol test because it was totally unexpected and in each of the instances served to reinforce the experience of the incompatibility of the drug and alcohol.

Tests were made to determine whether this reaction to after-shave lotion was due to alcohol being absorbed through the skin or to the absorption of alcoholic vapor by the mucous membranes. The abdomen was sponged freely with 70% alcohol as in preparation for surgery. While this was being done, the patients compressed their nares to prevent the contact of the alcohol vapor with the mucous membrane of the nasal passages. Within five minutes, both patients experienced a very mild, transient sensation of warmth of the face. No other symptoms developed. Later, the patients were asked to drip 70% alcohol on their hands, place their hands close to the nares and inhale. Within five minutes, a definite sensation of warmth of the face, some general perspiration, and some scleral injection developed. The reaction persisted for about 10 minutes, and both patients agreed that the reaction was increased by the smell of alcohol. It would appear, therefore, that the mechanism of this mild reaction is due primarily to absorption of alcohol vapor rather than to any appreciable absorption through the skin.

This clinical experience is being reported because it is believed that a similar mild tetraethylthiuramdisulfide-alcohol reaction could be produced by other commercially used products, such as hair tonics or cosmetic preparations. The mild reaction produced may be salutary as a reinforcement of the conditioning; on the other hand, it is possible that in certain situations such a reaction could cause considerable embarrassment and discouragement in a person who is finding it difficult to face his problems without the use of alcohol.

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TROPHIC VS. TROPIC

To the Editor:—Although I have not noticed "trophic" and "tropic" used incorrectly in THE JOURNAL, I would like to point out that they are often misused. Would it not be possible to have a unified nomenclature in using the respective terms? In articles dealing with female endocrinology one often encounters the expressions "gonadotrophic" or "luteotrophic" hormone. It has never occurred to most of the authors that this is a misnomer. They derive the second part of the words in question from the Greek *trephein*, which means to feed or to nourish. This appears in expressions like "atrophy or atrophic" or "hypertrophic," where it simply means that a certain part is either undernourished or overnourished; however, the words I am speaking of should read "gonadotropic or luteotropic," since these words are derived from the Greek *trepein*, which means to drive, change, or turn into. Therefore, it is understood that the pituitary gland producing these hormones does not "nourish" the ovary but that its hormones induce a change of the ovarian structure, namely, either follicle formation or transformation of the ruptured follicle into a corpus luteum.

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CANCER OF THE LUNG AND CIGARETTES

To the Editor:—In my article on bronchogenic carcinoma in THE JOURNAL (**148**:691 [March 1] 1952), I regret that I misquoted from Doll and Hill's report in the *British Medical Journal* (2:739, 1950) concerning the number of cigarettes smoked by patients with cancer of the lung. Instead of the statement "11.6% [of a series of patients with cancer of the lung] smoked 500,000 cigarettes or more a year," it should be that "7.6% of patients with cancer of the lung have smoked more than 500,000 cigarettes up to the time of the discovery of the cancer."

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BUREAU OF LEGAL MEDICINE AND LEGISLATION

MEDICOLEGAL ABSTRACTS

Evidence: Need for Physician Expert Witness to Be Licensed in State.—The plaintiff sued for damages resulting from an automobile collision. From a judgment in favor of the plaintiff, the defendant appealed to the Supreme Court of Wisconsin.

One of the physicians whom the plaintiff consulted was a resident and licensed practitioner in the State of Minnesota, but not in Wisconsin. The Wisconsin medical practice act provides that a person who is not licensed to practice in the State shall not testify in a professional capacity as a physician. The defendant therefore contended that this physician's testimony should not have been admitted in evidence. Another section of the medical practice act, however, excepts from its provisions physicians of other states in actual consultation with resident licensed practitioners of the State of Wisconsin.

It is true, said the Supreme Court, that Dr. Thorsen was engaged in practice in St. Paul, Minnesota and was not licensed to practice in Wisconsin, but it does appear that Dr. Ihle, who was treating the plaintiff, is licensed to practice in Wisconsin, and that he sought the assistance of Dr. Thorsen when he determined that his patient needed the attention of one engaged in Dr. Thorsen's specialty. A complete history of the patient's condition was sent to Dr. Thorsen when the arrangement was made under the advice of her physician for her to consult him. That physician, in this exchange made for the assistance of Dr. Ihle in treating the plaintiff, thus became a consultant. Dr. Thorsen treated the patient. He saw her at the Miller Hospital in St. Paul over a period of a week, prescribed for her, and gave her psychiatric treatments. There was a discussion of the case by him with Dr. Ihle, who was her Wisconsin physician at the time. The discussions were over the phone and in letters. As we have said, the patient was referred to Dr. Thorsen, by a competent qualified Wisconsin licensed practicing physician to whom Dr. Thorsen reported and with whom he consulted. The Supreme Court, therefore, concluded that the trial court properly, in the exercise of its discretion, admitted the evidence of Dr. Thorsen.

For other reasons, however, the judgment in favor of the plaintiff was reversed and the case remanded for a new trial.—*Landrath v. Allstate Ins. Co., 48 N. W. (2d) 485 (Wisconsin 1951).*

Hospitals for Profit: Liability of Physician-Owner.—The plaintiff sued for damages for injuries alleged to have been caused by the negligence of the defendant's agents, servants, and employees. From a judgment in favor of the defendant, the plaintiff appealed to the Supreme Court of Oklahoma.

The hospital in question was originally owned by the city of Altus, but, some time prior to the plaintiff's injury, the city leased the hospital to the defendant physician, who has since been operating, equipping, and managing it. The hospital is what is known as an "open staff" hospital, any licensed physician living within a reasonable distance of Altus being permitted to take his patients there for treatment. The defendant employs and staffs the hospital with nurses to assist the physicians in administering treatment to their patients. The plaintiff was suffering from an ailment that she was told by her physician, Dr. Ensey, was rheumatoid arthritis and was placed by him in the defendant's hospital for treatment. The plaintiff was given a heat wave treatment by means of a diathermy machine. Dr. Ensey, the plaintiff's physician, with the assistance of nurses furnished by the defendant, applied the heat to her back and set the dial at 250 ma. of current. He then left the hospital and instructed the nurse to cut off the heat in 20 minutes. At the same time, another nurse appeared to relieve this nurse and she was advised of the physician's instructions and told to disconnect the heat within 20 minutes. This nurse testified that she did within 20 minutes thereafter discontinue the heat. The plaintiff testified that, as the result of this treatment, her back and arm were severely burned. The contention of the plaintiff is that Dr. Ensey and the nurses who assisted him were agents, servants, and employees of the defendant.

We do not agree, said the Supreme Court. The undisputed evidence shows that Dr. Ensey applied the heat and directed the length of time it should remain applied. Assuming that the jury might have found under the evidence that the heat was applied at too great a degree of temperature, still, the defendant would not have been liable for Dr. Ensey's negligent act in so doing. The evidence shows without dispute that the relationship of physician and patient was created between Dr. Ensey and the plaintiff. Dr. Ensey was acting on his own account as a physician in prescribing and giving such treatment. He was not acting as an agent, servant, or employee of the defendant lessee nor was he acting under his control and direction. The defendant is, therefore, not liable for the negligence, if any, of Dr. Ensey in administering such treatment.

It is further contended by the plaintiff that the nurse in charge was guilty of negligence in not removing the pad from the plaintiff's back and discontinuing the heat application at the proper time and that, since the physician had then departed from the hospital, the nurse in charge was no longer under his direction, control, and supervision but was then acting as a general employee of the defendant under his supervision, direction, and control, and her negligence in failing to discontinue the heat treatment is chargeable to him. The evidence shows without dispute that the nurse, in doing what she did, was following strictly the directions of Dr. Ensey, the attending physician, and without any act of negligence on her part. If the heat was applied for too great a length of time it was because of negligence of Dr. Ensey in giving his instructions to the nurse and not because of any independent act of negligence on her part after the physician left the hospital. The defendant is not chargeable with Dr. Ensey's negligence. Accordingly, the judgment of the trial court in favor of the defendant physician was affirmed. *Van Cleave v. Irby, 233 P. (2d) 963 (Oklahoma, 1951).*

MEDICAL MOTION PICTURES

Oxygen Dosage and Technics: 16 mm., color, sound, showing time 28 minutes. Produced in 1951 by Audio Productions, Inc., 630 Ninth Avenue, New York 19, New York. Procurable on loan from Linde Air Products Company, 30 East 42nd St., New York 17.

This film demonstrates the application of various devices for use in the administration of oxygen. It shows oxygen piped in a hospital and delivered in cylinders and the use of pressure reducing valves in various types of inhalation apparatus. It pictures a tent using a large canopy covering the entire mattress, incubators, the use of various face masks, positive pressure masks, the nasal catheter, hoods, and even improvised funnels, bags, and gadgets to administer oxygen. The emphasis is on the administration of oxygen rather than on the medical indications for its use, although there is some mention as to what conditions are best treated by this method. One section shows the use of helium and oxygen for obstructions in breathing.

A great many facts, devices, and tricks in operation have been compressed into this short informative film; however, some details are omitted that would benefit personnel unfamiliar with the use of oxygen. For example, there is no mention made of the danger of inserting the catheter too far or not far enough. Mention is made of the necessity for analyzing oxygen content under hoods and tents. The film demonstrates this being done with a Beckman Analyzer. A classroom demonstration technique was used rather than actual patients. The photography, the selection of subjects, and the selection and display of apparatus are all well planned and executed. The film is recommended for use by anyone interested in the proper application of oxygen therapy whether at the skilled or unskilled level. It does not pertain to medical judgment on the use of oxygen. It is a film on the technique of the use of oxygen. It should be shown to all nurses.

MEDICAL LITERATURE ABSTRACTS

UNITED STATES

A.M.A. Am. Journal Diseases Child., Chicago

83:151-270 (Feb.) 1952

Differential Diagnosis of Oligophrenia. R. Gibson.—p. 151.
*Physiological Knock-Knee. T. V. Geppert.—p. 154.
Chronic Panniculitis with Leucopenia (Weber-Christian Syndrome). H. N. Sanford, D. F. Eubank and F. Stenn.—p. 156.
Organic-Aciduria, Decreased Renal Ammonia Production, Hydrophthalmos, and Mental Retardation: Clinical Entity. C. U. Lowe, M. Terrey and E. A. MacLachlan.—p. 164.
Renal Function Studies in Pediatrics: I. Renal Hemodynamics in Children with Sickle Cell Anemia. J. N. Etteldorf, A. H. Tuttle and G. W. Clayton.—p. 185.
Diarrhea of the Newborn: Report of Epidemic and Results of Treatment with Streptonycin. R. B. Scott, G. P. Brown and A. D. Kessler.—p. 192.
Ehlers-Danlos Syndrome: Report of Case with Suggestion of Possible Causal Mechanism. A. Kanof.—p. 197.
Early Descriptions of Congenital Pyloric Stenosis. H. R. E. Wallis.—p. 203.

Physiological Knock Knee.—The high incidence of knock knee between the ages of 1 and 6 years induced Geppert to investigate whether and to what extent knock knee is physiological in children at this age. He also decided that there should be a fairly accurate technique of measuring the distance between the medial malleoli in order to determine the need for treatment of pathological knock knee. If therapy is indicated, then comparative figures would reveal the success of the treatment. An attempt was made to establish normal values for each year by measuring children seen in his practice and in nursery schools. Measurements were made on 239 children, and in 7 the values exceeded the average so much that they were definitely abnormal. It was found that children of 3 years have the greatest deviation, and it is now felt that a distance of over 3.5 cm. at this age is evidence that a special shoe is indicated, with a wedge on the inner border.

American Heart Journal, St. Louis

43:1-160 (Jan.) 1952

Clinical and Physiological Correlations in Patients with Mitral Stenosis. V. B. M. Lewis, R. Gorlin, H. E. J. Houssay and others.—p. 2.
Morphology of Unipolar Leads Recorded at Septal Surfaces: Its Application to Diagnosis of Left Bundle Branch Block Complicated by Myocardial Infarction. D. Sodi-Pallares and M. I. Rodríguez.—p. 27.
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Some Factors Affecting Clearance of Na^{24} from Human Muscle. L. H. Wisham and R. S. Yallow.—p. 67.
Clinical and Cardiac Catheterization Findings Compatible with Ebstein's Anomaly of Tricuspid Valve: Report of Two Cases. B. van Lingen, M. McGregor, J. Kaye and others.—p. 77.
Ventricular Tachycardia Following Administration of Quinidine. D. G. Wetherbee, D. Holzman and M. G. Brown.—p. 89.
*Ligation of Vena Cava in Treatment of Heart Failure. P. Cossio.—p. 97.

Ligation of Vena Cava in Heart Failure.—Cossio states that in 1948 he and Perianes proposed ligation of the inferior vena cava below the renal veins to control left cardiac failure that no longer responds to medical treatment, including absolute rest in a suitable position, low sodium diet, and administration of digitalis and mercurial diuretics. In a later report, based on observations in a larger series, they attributed the disappearance of the edema in the lower limbs after ligation of the vena cava to the improved lymphatic drainage of the lower half of the body as a consequence of the drop in venous pressure in the upper half, which, in turn, was caused by improvement of cardiac function. On the other hand, they ascribed the appearance of edema in the lower limbs after the ligation to blockage of the lymphatic return by mechanical damage or inflammation of the tributary vessels and lymph nodes. The author mentions others who have employed ligation of the vena cava, and then summarizes his own observations in a total of 90 cases in which he performed ligation of the inferior vena cava for uncontrollable heart failure. The surgical mortality was initially 25%, but it was soon reduced to 6%. Early improvement was observed in 70% of the patients and was maintained for months or even years in 56% if medical treatment was continued. The early improvement is attributed to reduction of blood return to the heart, and the later improvement to formation of a lake of blood, with a slower return in the recumbent position, and also to elimination of the source of microemboli.

American J. Digestive Diseases, Fort Wayne, Ind.

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Hyperinsulinism—Factor in Rheumatoid Arthritis. E. M. Abrahamson.—p. 1.
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Clinical Studies of Blood Lipid Metabolism: I. Normal Blood Lipid Variations of Phospholipids, Neutral Fats, Total Lipids, and Lipid Fraction Percentages. A. A. Goldbloom.—p. 9.
Sigmoido-Rectal Intussusception and the Unstable Colon. E. Granet.—p. 19.
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American Journal of Hygiene, Baltimore

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Id.: II. Observations During Influenza A-Prime Epidemic. G. Meiklejohn, C. H. Kempe, W. G. Thalman and E. H. Lennette.—p. 12.
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Studies of Distribution of Poliomyelitis Virus: VI. In Small Community in Epidemic Area. G. C. Brown, J. D. Ainslie, A. G. Gilliam and others.—p. 49.
Effect of Drugs on Excretion of Theiler's Virus (TO) by Mice. G. A. LoGrippo, D. P. Earle Jr., B. B. Brodie and others.—p. 55.
Effect of Mercurial Compound in Suppressing Intestinal Carriage of Theiler's Virus (TO) in Mice. G. A. LoGrippo, D. P. Earle Jr., I. Graef and R. Ward.—p. 70.
Serologic Studies of Corynebacterium Diphtheriae: III. Cultural Grouping and Serologic Typing of Diphtheria Field Cultures from Pacific Coast Region of the United States. V. J. Freeman and G. H. Minzel.—p. 74.
Studies of Coxsackie Viruses: Laboratory Aspects of Group Viruses. E. A. Beeman, R. J. Huebner and R. M. Cole.—p. 83.
*Immune Responses in Human Volunteers upon Oral Administration of Rodent-Adapted Strain of Poliomyelitis. H. Koprowski, G. A. Jervis and T. W. Norton.—p. 108.
*Poliomyelitis in Pregnancy. G. W. Anderson, G. Anderson, A. Skaar and F. Saadler.—p. 127.
Preliminary Evaluation of Immunizing Power of Chick-Embryo 17D Yellow Fever Vaccine Inoculated by Scarification. G. W. A. Dick.—p. 140.

Immune Responses in Humans to Orally Administered Poliomyelitis Virus.—The TN strain of poliomyelitis virus, which was used in the studies described here, displayed a remarkably low virulence for rhesus monkeys when injected intracerebrally.

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Titles marked with an asterisk (*) are abstracted.

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Material used for human feedings was prepared by giving viable suspensions of virus intracerebrally to cotton rats. After showing signs of paralysis the animals were killed, and their brains and spinal cords were removed aseptically. A 20% tissue suspension by weight was prepared with 5% aqueous dextrose used as diluent. The material was then placed in glass ampuls, which were flame sealed and stored in the frozen state. After thawing, the infectious material was given orally to the volunteers either alone or in milk or corn syrup. For the mouse neutralization tests, the MEF1 strain of poliomyelitis virus at the 64th hamster passage was used. Three of the 20 volunteers possessed neutralizing power against the MEF1 strain of virus prior to ingesting the TN strain, and the immunological status of two other volunteers proved difficult to determine by neutralization test, but the serums of the other 15 volunteers had no neutralizing power against MEF1 strain. Twelve of the 15 excreted virus in their stools at some time later than four days after ingestion of the TN strain. Neutralizing antibodies were found in the serum of all 15 volunteers. Observations on the subjects whose serum contained neutralizing antibodies before the ingestion of the virus suggests that the presence of circulating neutralizing antibodies does not preclude establishment of a carrier state with homologous virus. Furthermore, some showed a second carrier phase, which proves that the carrier state is compatible with the presence of a high antibody level, and it is not, as has been suggested by others, conditioned by a decline in serum antibody level. A discussion of oral administration of TN virus in terms of an immunizing process is regarded as premature until the safety of the procedure has been established. However, one may speculate upon the possibility that feeding of the TN strain to nonimmune human beings may induce a state of serological immunity of such magnitude that it would check invasion of the central nervous system by a homotypic virus, even when an intestinal carrier state results.

Poliomyelitis in Pregnancy.—There is a general belief that pregnancy increases susceptibility to poliomyelitis, and it has been suggested that the increased susceptibility is connected with endocrine imbalance. The 1946 poliomyelitis outbreak in Minnesota furnished an opportunity to study a relatively large number of cases of poliomyelitis associated with pregnancy and to gather data regarding menstrual histories that might reflect subclinical endocrine imbalances. The records of 75 pregnant women who had poliomyelitis are analyzed. Eight of these died. There was no evidence of a greater severity of the infection among pregnant women than among a comparable group of nonpregnant married women simultaneously attacked. The attack rate among pregnant women is higher than among an estimated control group of nonpregnant married women. The higher attack rate in pregnancy cannot be explained on the basis of greater degree of exposure to infection. There was a slight concentration (and especially of serious cases) in the second to fifth month. There was a predominance of male fetuses among these patients, especially those attacked in the early stages of pregnancy. The rate of congenital abnormalities was not unduly high among the children born to these women who had poliomyelitis during pregnancy.

American Journal of Ophthalmology, Chicago

35:1-166 (Jan.) 1952

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American Journal of Public Health, New York

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Am. J. Roentgenol. & Rad. Therapy, Springfield, Ill.

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Degenerative Osteoarthritis of Hip Joint: Pathogenesis of Enlarged Femoral Head (Coxa Magna) and Defective Acetabulum. T. Horwitz. —p. 95.
Case of Osteogenesis Imperfecta Diagnosed in Utero. H. W. Frerking and O. C. Zink.—p. 103.
New Roentgen Sign of Fetal Death. S. N. Tager.—p. 106.

Metabolism of Radioactive Iodine.—The effects of varying degrees of cardiac failure on the metabolism of radioactive iodine (I^{131}) were studied by observation of the soft tissue retention, thyroid gland uptake, and urinary excretion in 20 patients with severe cardiovascular disease who had been given a 50 μc carrier-free dose of I^{131} orally before breakfast on the initial day of study. Of the 20 patients, 14 had gross evidence of cardiac failure, while the remaining 6 had no clinical edema at the time of study. The results in this group of patients were compared with those obtained in 44 patients showing no significant cardiac disease; 23 had varying levels of total thyroid function as judged by total urinary I^{131} excretion. Certain abnormalities of I^{131} metabolism were characteristic in the patients with cardiac decompensation. These included pronounced soft tissue retention of I^{131} from 24 to 36 hours after ingestion of the material, together with deficient I^{131} concentration in the thyroid gland during this time. In addition, certain changes in the pattern of urinary excretion of I^{131} throughout the period were noted. Attention is called to the fact that these changes in the metabolism of I^{131} may occasionally mask the presence of latent thyrotoxicosis in a patient with cardiac disease. In still other situations occult edema as a prodrome of gross cardiac decompensation may be detected by I^{131} tracer studies before clinical evidence appears.

Detection of Gastric Cancer by Photofluorographic Methods.—In 29 months 10,000 photofluorographic gastrointestinal examinations were made at the Johns Hopkins Hospital in dispensary patients, 4,584 men and 5,416 women, aged over 40. Six exposures were made for each patient, all with the patient in the recumbent position, the average fasting time being approximately three to four hours, and the total amount of barium sulfate, water, and chocolate malt mixture being 6 oz. (180 cc.).

Of the 10,000 patients, the stomach was visualized well enough in 9,072 (90.7%) to warrant a diagnostic interpretation, while in the remaining 928 cases (9.3%) the stomach was inadequately demonstrated. Of the 928 patients, 528 (5.3% of all patients studied) obtained unsatisfactory results because of the presence of excessive food within the stomach, 345 (3.5%) because of technical errors, and 55 (0.5%) because of excessive obesity. Of the 9,072 patients with satisfactory miniature studies, the stomach was interpreted as normal in 8,219 (90.6%), while in 853 (9.4%) the stomach appeared to be abnormal. The duodenal bulb was thought to be normal in 4,532 patients (50%) and abnormal in 200 (2.2%), and was inadequately visualized in 4,340 (47.8%). Of the 9,072 patients with satisfactory miniature studies, 1,209 (13.3%) also received standard gastrointestinal examinations, while in 7,863 patients (86.7%) the miniature studies were not checked by regular gastrointestinal series; of the latter the stomachs of 7,462 were thought to be normal and of 401 to be abnormal. In 185 of the latter patients the presence of neoplastic disease could not be completely excluded. In the 1,209 patients comparison of the gastric findings of regular and miniature studies showed that in 732 patients (60.6%) the stomach was interpreted as normal on both the regular and the miniature studies. In 126 patients (10.4%) the stomach was observed to be abnormal on both studies, and in 307 patients (25.4%) it was thought to be abnormal on the miniature study, only to have a standard gastrointestinal series reveal a normal stomach. This appears to be an excessively high error but these patients were much more likely to receive the standard series than were those in whom the miniature study was reported as showing a normal stomach. If one includes all of the satisfactory miniature studies, the false positive error falls to 3.3% and this is felt to be a more accurate estimate of the situation. There were only 17 patients in whom the miniature studies were interpreted as showing a normal stomach, only to have the standard examination reveal the presence of gastric pathology. Any apparent abnormality on the miniature study should be checked with a standard gastrointestinal study before a definite opinion is reached regarding the status of the stomach. The number of persons with asymptomatic gastric cancers or their precursors is relatively small, being approximately 1 per 476 examinations in the authors' series. Only a few of these could be persuaded to submit to surgery prior to development of symptoms. It appears that the general public must receive further education concerning the gastric cancer problem before photofluorography will be successful in reducing the death rate from malignant gastric growths. If only those patients are considered in whom potentially benign gastric lesions detected by the miniature studies were actually confirmed by standard examinations, the over-all incidence is 1.3%, or 1 per 79 examinations. The chief drawback to use of the photofluorographic method for mass surveys is the considerable number of cases in which the duodenal bulb is inadequately visualized for diagnostic purposes. Currently efforts are being made to reduce this number by prolonging the interval between the taking of the opaque medium and the filming process. With the photofluorographic method it should be possible to greatly reduce the number of standard examinations in large institutions where considerable numbers of gastrointestinal examinations are requested by the clinicians, thus resulting in a considerable saving in time and expense to the clinician and patient.

Annals of Western Medicine & Surgery, Los Angeles

6:1-68 (Jar.) 1952

*Range of Usefulness of Commercial Stainless Steel Clotns in General and Special Forms of Surgical Practice. W. W. Babcock.—p. 15.
Toxic Reactions to Tetramycin: Report of Case. R. X. DeMangus. —p. 24.
The Law of Abortion. L. J. Regan.—p. 26.
Painful Conditions Simulating Heart Disease. R. W. Langley.—p. 49.

Stainless Steel Cloths in Surgical Practice.—Annealed stainless steel wire has been used in surgery since 1929. In 1947 Babcock inquired into the possibility of obtaining the wire in the form of a mesh or screen for surgical use, and various fine steel cloths were tested by implantation into dogs and then were tried clinically. It is important that only the alloys 18—8 stainless steel be used, as other stainless or rustless alloys at present available cause undesirable tissue reaction or, like vitallium, lack ductility or tensile strength. Stainless steel cloth may be repeatedly sterilized by boiling or by superheated steam without injury. Previous to sterilization a degreasing solution should be applied, followed by scrubbing with a brush and soap and thorough rinsing. Sharp projecting points of wire should be trimmed off or rolled back before implantation. Of the soft and flexible screens classified grade 1, five different types have been selected and are used for abdominal hernias or to cover defects in the thoracic wall. They may be placed against omentum, intestines, lung, or heart, and may be used to surround and reinforce large blood vessels and aneurysms and to repair defects in the diaphragm, pleura, or dura, as well as to replace or reinforce defective subcutaneous tissue. Thin but stiffer forms of mesh classified as grade 2 may be used to cover defects on the trachea and larynx, or to replace cartilage and restore contours to the nose, ears, and eyelids, to form a new floor for the orbit. Grade 3 includes the thicker and more rigid screens that are adequate to cover defects in the skull and to bridge bony defects in various other parts of the skeleton. It has been suggested that serious damage may result from the action of solar, roentgen, or diathermic radiation on parts that contain embedded metal, but the author says that many patients having buried wire sutures or screen in the abdominal wall or cavity have been exposed to roentgen rays without evidence of damage. He admits, however, that conditions may be different if a large plate of tantalum or alloy steel fills a large defect in the skull, lying close to the brain. In such a case diathermy should not be used, and exposure to the hot sun or to x-rays should be brief.

Circulation, New York

5:1-160 (Jan.) 1952

*Chest Pain in Association with Pulmonary Hypertension: Its Similarity to Pain of Coronary Disease. W. N. Viar and T. R. Harrison.—p. 1.
Study of Digitalis-Like Action of Thevetoidin in Man. I. Chavez, R. Méndez and L. O. Chait.—p. 12.
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*Effect of 1-Hydrazinophthalazine in Hypertension. H. A. Schroeder. —p. 28.
Effects of Valsalva-Like Maneuver upon Circulation in Normal Individuals and Patients with Mitral Stenosis. H. Goldberg, E. I. Elisberg and L. N. Katz.—p. 38.
Epicardial Electrocardiograms Recorded in Course of Seven Cases of Heart Surgery. G. J. Carouso, H. A. Chevalier, B. I. Latscha and J. Lenègre.—p. 48.
Distribution of Body Fluids in Congestive Heart Failure: IV. Exchanges in Patients, Refractory to Mercurial Diuretics, Treated with Sodium and Potassium. J. R. Elkinton, R. D. Squires and L. W. Bluemle Jr. —p. 58.
Size of Heart During Course of Essential Hypertension. M. Kleinfeld and J. Redish.—p. 74.
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ATHEROSCLEROSIS: A SYMPOSIUM

Experimental Atherosclerosis. L. N. Katz.—p. 101.
Human Atherosclerosis and Diet. A. Keys.—p. 115.
Blood Lipids and Human Atherosclerosis. J. W. Gofman, H. B. Jones, T. P. Lyon and others.—p. 119.

Chest Pain in Pulmonary Hypertension.—Pain of pulmonary hypertension, which resembles the pain of coronary disease in nature and in the tendency to be initiated by physical exertion, can usually be differentiated if the clinical features of the syndrome are thoroughly understood. The existence of a condition capable of causing pulmonary hypertension offers a clue to correct diagnosis. The commonest underlying conditions are (1) mitral lesions, usually stenotic but occasionally regurgitant; (2) primary diffuse lung disorders, especially asthma, emphysema, and bronchiectasis; (3) pulmonary arterial disorders, oftenest embolism; and (4) congenital malformations of the heart leading to increased pressure in the pulmonary artery. Other guides may be long-standing cough, cyanosis, associated dyspnea, pain on breathing, variable duration of pain, clinical evidence of

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right ventricular hypertrophy, electrocardiographic changes, evidence of tissue destruction, and effects of oxygen and drugs. Consideration of these factors should aid in differentiation of the two types of pain. The prognosis in pulmonary hypertension is better than in coronary disease: attacks of pain have a less ominous significance, and sudden and unexpected death is less likely to occur. Treatment is essentially that of the causative condition; oxygen and aminophylline administered rectally may prove beneficial. The similarity between the pain of pulmonary hypertension and that of coronary disease is probably due to the fact that the afferent nerves from the pulmonary artery enter the nervous system by the same pathways as those from the heart. The pain apparently originates in the pulmonary artery itself, resulting from distention of the vessel.

Effect of 1-Hydrazinophthalazine in Hypertension.—A true antihypertensive drug should lower blood pressure without affecting the myocardium adversely, decreasing renal blood flow, or altering blood volume or viscosity. 1-Hydrazinophthalazine and 4-methyl-1-hydrazinophthalazine met these requirements when given experimentally to 50 patients with arterial hypertension. They are relatively nontoxic and are the most effective hypotensive agents so far encountered for practical clinical use, but their effectiveness is only partial and varies with the type of hypertension. The most pronounced effects were seen in neurogenic hypertension, some cases of malignant hypertension, and after lumbodorsal sympathectomy; effects were minimal in cases of severe renal hypertension when renal function was good. Serious chronic toxic manifestations were not observed, even in patients receiving the drugs for as long as eight months. Side-reactions consisted of headache, tachycardia, postural hypertension (sometimes severe), nausea and vomiting, and, in seven serious cases, cerebral symptoms ranging from mild anxiety and depression to acute anxiety or severe depression and coma (in two severely uremic patients). Most of these reactions either diminished or disappeared while the drugs were being given; in only four cases of headache was it necessary to discontinue the treatment. Dosage consisted of 50 to 150 mg. given orally every four to six hours in hospitalized patients and three to five times a day to outpatients. The average diastolic blood pressure drop was 20 mm. Hg or more in 35 cases, but in only a few of the mildest cases were normotensive levels sustained.

Neurology, Minneapolis

2:1-82 (Jan.-Feb.) 1952

Syndrome of Periodic Paralysis. W. W. Hofmann.—p. 1.
Syndrome of Anterior Spinal Artery. A. T. Steegmann.—p. 15.
Spread of Sensory and Motor Loss After Nerve Injury. M. Kelly.—p. 36.
Face-Hand Test as Diagnostic Sign of Organic Mental Syndrome. M. Fink, M. Green and M. B. Bender.—p. 46.
Use of Benadryl for Symptomatic Relief of "Thalamic Pain." R. W. Barris.—p. 59.

New England Journal of Medicine, Boston

246:1-40 (Jan. 3) 1952

*Sex Hormones in Advanced Breast Cancer. E. F. Lewison and R. G. Chambers.—p. 1.
Malignant Hypertension with Unilateral Renal-Artery Occlusion. H. L. Goodman.—p. 8.
Role of the Internist in a Mental-Hygiene Clinic. S. P. Seigle, I. Schnap and R. A. Castagno.—p. 12.
Effect of Depo-Heparin on Prothrombin Time, with Observations on Combined Use of Heparin and Dicumarol. J. B. Holyoke and H. J. Wheelwright Jr.—p. 15.
Artificial Kidney. J. P. Merrill.—p. 17.

Sex Hormones in Advanced Breast Cancer.—This paper describes observations on 80 women with advanced breast cancer who were treated with androgens or estrogens for at least three months. A favorable subjective response was obtained in 46 of 57 patients receiving androgens and in 21 of 40 receiving estrogens. Bone metastases showed objective improvement in 8 of 32 patients receiving androgens and in 3 of 11 patients receiving estrogens. Soft tissue lesions showed objective improvement in 17 of 48 patients receiving androgens and in 12 of 34 receiving estrogens. The clinical response to sex steroids is unpredictable. The estrogens appear to be most effective in postmenopausal women, whereas the androgens may be of value regardless of age. Optimum response requires administration of an adequate total dose over a sufficient length of time. The sex hormones are not a "cure" for breast cancer, but they do offer gratifying benefits in patients beyond the scope of surgery or radiotherapy.

New York State Journal of Medicine, New York

52:1-112 (Jan. 1) 1952

Control of Communicable Disease in Hospital Nurseries for Newborn: Progress Report, New York State Plan. R. F. Korns, E. R. Schlesinger and M. Y. Phaneuf.—p. 39.
Differential Use of Health Resources by Rural People. O. F. Larson and D. G. Hay.—p. 43.
Recent Trends in Tuberculosis in New York City. A. B. Robins.—p. 50.
What Physician Should Know About Current Status of Dental Caries Prophylaxis. D. B. Ast.—p. 57.
Symposium: Community Planning and Evaluation of Pediatric Services Midcentury White House Conference on Children and Youth: Health Aspects. A. D. Kaiser.—p. 63.
Four Years After. G. A. Wheatley.—p. 68.
Adolescent Drug Addiction. J. M. Toolan, P. Zimmering and S. B. Wortis.—p. 72.
Gastrointestinal Studies in Paraplegic: I. Bowel Management in Paraplegia. K. C. Keeler and H. A. Rusk.—p. 75.
Rehabilitation in Institutional Geriatrics: Preliminary Report. L. Dobrin.—p. 81.
Modification of Hofmeister Gastrectomy Operation. M. Weinstein and M. Roberts.—p. 86.
Analgesic Action of Subdamine. Effect of Subdamine on Pain Threshold and in Treatment of Idiopathic Glossodynia. A. H. Kutscher.—p. 91.

North Carolina Medical Journal, Winston-Salem

12:573-628 (Dec.) 1951

Public Health Aspects of Civil Defense. C. P. Stevick and J. W. R. Norton.—p. 573.
Cardiac Arrest During Anesthesia and Surgical Operations. T. C. Bost.—p. 579.
Malignant Adenomas of Colon and Rectum (Adenoma Malignum). R. S. McElwee and S. W. Moore.—p. 586.
Enterogenous Cysts of Cecum. F. M. S. Patterson.—p. 591.
Myositis Ossificans with Report of Case in Paravertebral Muscle. B. Creech and J. U. Gunter.—p. 595.
Clinical Aspects of Treatment of Syphilis. G. E. Koury.—p. 600.
Pupillary Changes Associated with Diabetic Neuropathy. W. D. Pryor.—p. 605.
Diagnosis of Tumors of Uterine Canal. W. B. Norment.—p. 607.

13:1-52 (Jan.) 1952

Coronary Occlusion Before Age of Forty: Report of 23 Cases. J. G. Smith.—p. 1.
Pains in Chest—"True or False." R. L. McMillan.—p. 9.
Some Comparisons of Neuropsychiatric Casualties in Recent American Wars. W. E. Wilkinson, G. F. Southerland and W. C. Betts.—p. 11.
Myxedema: Controllable Condition Which is Frequently Overlooked. G. T. Harrell.—p. 15.
Cortisone and Aureomycin in Treatment of Case of Rocky Mountain Spotted Fever. W. C. Arney.—p. 20.
Body Potassium Loss During Therapy with ACTH and Cortisone. J. K. Aikawa and J. H. Felts Jr.—p. 22.
Use of Oral Vasoconstrictors in Rhinology. J. S. Gordon.—p. 24.
Physiologic Correction of Internal and External Nasal Deformities. C. N. Patterson.—p. 29.
*Carbon Dioxide Retention During Oxygen Therapy. J. B. Hickam, H. O. Sieker, W. W. Pryor and J. M. Ryan.—p. 35.
*Black Widow Spider Bite Syndrome. L. J. Taubenhaus.—p. 37.
Complications of Poison Ivy (Rhus Toxicodendron) Dermatitis. S. W. Barefoot.—p. 40.

Carbon Dioxide Retention During Oxygen Therapy.—The lungs have the function of eliminating carbon dioxide as well as of absorbing oxygen. Oxygen therapy can increase oxygen absorption, but there is no similarly effective means of facilitating carbon dioxide elimination. In patients who become accustomed to high tensions of carbon dioxide, the respiratory center is no longer normally sensitive to this gas; instead, much of the respiratory stimulus is being supplied by the low arterial blood oxygen tension. When this stimulus is abruptly removed by oxygen therapy, respiration is slowed, and the blood carbon dioxide tension rises rapidly. The methods used in the analysis of arterial blood gases were described elsewhere by the authors; in this report they present four patients in whom the blood carbon dioxide became extremely high during oxygen therapy. These patients had mental disturbances, lethargy, and coma. Carbon dioxide poisoning can easily occur during prolonged oxygen therapy, and its recognition can clarify situations that may appear quite puzzling.

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Black Widow Spider Bites.—The black widow spider (Latrodectus mactans) has been reported in all but seven states. The syndrome caused by the sting of this insect should be recognized particularly by physicians in rural practice, the author having observed 18 cases during three years' of rural practice in southeastern North Carolina. The belief that most patients are bitten by this spider while using a privy was not borne out by the author's observations that many were bitten on the upper extremities while picking up sticks and firewood, and on the toes while putting on shoes that had not been worn recently. Symptoms usually start with severe pains in the bones, muscles, and joints, and spread to the back and abdomen. In most cases the abdominal pain is so severe that it masks all other pain. The abdomen is frequently board-like, resembling that seen with a ruptured peptic ulcer, and many patients have been mistakenly subjected to surgery. The fact that the patient may not recall the sting makes the diagnosis difficult. The author feels that patients with an acutely painful abdomen should be asked about having received a sting. The latent period after the bite varies from 15 minutes to 4 hours. Calcium gluconate or magnesium sulfate given intravenously are excellent drugs for relieving pain and spasm, but their effect is only temporary and they do not shorten the duration of the illness. If this treatment is used, the alternate injection of 10 cc. of a 10% solution of calcium gluconate and 2 cc. of a 50% solution of magnesium sulfate is probably better than administration of only one of these drugs. The author uses the therapeutic method recommended by Miller. On diagnosis 10 cc. of a 10% solution of calcium gluconate or 2 cc. of a 50% solution of magnesium sulfate is given intravenously to relieve the pain. Then the patient is tested for serum sensitivity, after which one vial of antivenin is given intramuscularly. Usually this is all that is necessary, but occasionally more antivenin is needed. The use of specific antivenin is the best treatment. It avoids prolonged suffering and makes hospitalization unnecessary.

Oklahoma State Medical Assn. J., Oklahoma City

45:1-44 (Jan.) 1952

Penetrating Abdominal Injuries. C. M. O'Leary.—p. 4.
Use of Banthine in Treatment of Duodenal Ulcers. T. E. Johnston.—p. 7.
Role of Potassium in Body. J. B. Morey.—p. 10.
*Treatment of Myocardial Infarction Due to Coronary Thrombosis: Preliminary Report. W. T. McCollum.—p. 15.

45:45-86 (Feb.) 1952

Spontaneous Rupture of Esophagus. R. L. Anderson.—p. 49.
Management of Urological Problems in General Practice. E. N. Lubin.—p. 53.
Face Injuries. G. H. Kimball.—p. 56.
Local Anesthesia in Obstetrics. J. L. McKelvey.—p. 58.
Recent Advances in Diagnosis and Treatment of Cancer. H. A. Burnett.—p. 61.

Treatment of Myocardial Infarction.—This report is based on 80 cases in which the diagnosis of myocardial infarction was based on electrocardiographic records of definite breakdown in the QRS complex. After the diagnosis had been established, the patient was given 16 mg. of morphine sulfate and 0.43 mg. of atropine sulfate either intravenously or subcutaneously, depending on the severity of the pain. When necessary, this dose was repeated. Quinidine sulfate in doses of 0.2 gm. was given orally every four hours, day and night. At the end of two weeks the dosage was reduced to 0.2 gm. every four hours during the day and 0.4 gm. at bedtime. The anticoagulant effects of bishydroxycoumarin were supplemented by those of aqueous heparin in 50 mg. doses intravenously every four hours, day and night, for the first 48 to 72 hours, until the prothrombin time had time to reach a therapeutic level. The initial dose of bishydroxycoumarin was 300 mg. on admission. Further doses were adjusted on the basis of daily determination of prothrombin time. The prothrombin time was maintained between two and three times the normal time. The administration of bishyroxycoumarin was usually continued until the patient became ambulatory. Patients were kept in bed until the electrocardiographic record revealed healing of the lesions, the sedimentation rate returned to normal, and the pulse and blood pressure were stabilized. Oxygen was given routinely at a rate of 5 liters per minute by nasal catheter. Since the mortality is reportedly twice as high in patients in whom the systolic blood pressure is below 100 mm. of mercury, McCollum gave these patients desoxyphedrine in 5 mg. doses, not exceeding 25 mg. per day. A decided fall in pressure was treated with a dose as high as 10 mg. intramuscularly at once and then 5 mg. doses every four hours for the first 24 hours, reducing the dosage in the second 24 hour period to the above mentioned total daily dose. The blood pressure routinely improved by 15 to 20 mm. Hg. To reduce the exertion involved in defecation, mineral oil is given at bed time or enemas are given if needed. The diet was liquid for the first two or three days and the sodium intake was restricted to 200 mg. per day. Ten of the 80 patients died. This over-all mortality rate of 12.5% included patients with previous infarctions; in those experiencing the initial myocardial infarction the mortality rate was 7.5%. The author feels that this low rate proves the adequacy of the treatment.

Public Health Reports, Washington, D. C.

67:1-120 (Jan.) 1952. **Partial Index**

Susceptibility of Anopheles Quadrimaculatus to Korean Vivax Malaria. M. D. Young and R. W. Burgess.—p. 14.
Venereal Disease Control Program in Transition. T. J. Bauer.—p. 17.
National Morbidity Reporting. C. C. Dauer.—p. 21.
Fluoridation of Municipal Waters, American Dental Association Symposium. F. S. McKay, A. P. Black, M. E. Nicholson and F. A. Bull.—p. 36.
Leadership and Conditions of Organizational Effectiveness. D. McGregor.—p. 42.
Observations on Epidemiology of Poliomyelitis. W. T. Fales and M. Taback.—p. 47.
*Trichophyton Tonsurans Ringworm—New Public Health Problem. L. K. Georg.—p. 53.
Aquatic Invertebrates as Indicators of Stream Pollution. A. R. Gaufin and C. M. Tarzwell.—p. 57.
Health Departments and the Housing Problem. R. J. Johnson.—p. 65.
Evaluating Health Education. A. L. Knutson.—p. 73.
Studies in Penicillin Treatment of Syphilis. R. C. Arnold, J. C. Cutler, R. D. Wright and S. Levitan.—p. 78.

Trichophyton Tonsurans Ringworm: New Public Health Problem.—For the past 8 to 10 years the common agent of ringworm of the scalp in the United States has been Microsporum audouini. In some sections of the country it is the cause of 80 to 90% of the cases of ringworm of the scalp. Now, however, ringworm infections due to Trichophyton tonsurans are becoming an increasingly important public health problem in the United States. Isolations of this fungus from clinical cases of ringworm of the scalp, as well as from ringworm of the glabrous skin and nails, are made more frequently than heretofore in certain sections of the country, especially in Texas and other southwestern states. The author of this paper found that in New York City T. tonsurans infections occurred chiefly among Puerto Ricans who had recently immigrated to the United States. Scattered cases have been reported from many other states. Since Mexico is an endemic area for T. tonsurans infections, it seems probable that the disease has been spreading into Texas and the southwestern states from this area. It is possible that T. tonsurans may produce a widespread epidemic in the school children in the United States in a fashion similar to that of epidemic ringworm due to M. audouini. The problem would be more difficult, however, because the infections occur in both children and adults. They are more difficult to detect and usually are more refractory to treatment.

Review of Gastroenterology, New York

18:833-936 (Dec.) 1951

Clinical Appraisal of Liver Function Tests. H. A. Rafsky, M. Weingarten and C. I. Krieger.—p. 845.
Gastroileostomy. J. M. Miller and R. J. Lipin.—p. 854.
Hemorrhoids: Etiology, Pathology and Treatment. (Part II). R. V. Gorsch.—p. 859.
Varices of Esophagus. E. Boros.—p. 878.
Giant Echinococcus Cyst of Spleen: Case Report. F. W. Bancroft.—p. 882.
Gastric Resection Followed by Stricture of Common Duct: Case Report. F. W. Bancroft.—p. 888.
Primary Ulcer of Jejunum. M. Rich and M. M. Sayet.—p. 895.
Results of Treatment of Bleeding Peptic Ulcer. G. B. Packard.—p. 903.
Perforations of Small Intestine Due to Nonpenetrating Trauma. B. J. Ficarra.—p. 908.

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South Carolina Medical Assn. Journal, Florence

48:1-26 (Jan.) 1952

Treatment of Duodenal Ulcer and Functional Bowel Disease with Kolantyl, New Antispasmodic Compound: Preliminary Clinical Notes. B. N. Miller.—p. 1.
Rheumatic Carditis. J. A. Boone.—p. 6.
Painful and Painless Anorectal Lesions. L. Banov Jr.—p. 8.

48:27-56 (Feb.) 1952

Report of Case with Reference to Hazards of Sensitization Arising from Topical Medication. V. Moseley and S. Prystowsky.—p. 27.
Relief of Impotency by Cartilage Implants: Presentation of Technic. B. S. Chappell.—p. 31.
Dietary Problems in South Carolina. A. M. Moser.—p. 34.

South Dakota J. Med. & Pharmacy, Sioux Falls

4:317-342 (Dec.) 1951

Serum Protein Abnormalities Observed in Orthopedic Patients. R. E. Van Demark.—p. 317.
Eruptive Diseases of Contagious Nature. A. L. Hoyne.—p. 318.
Porphyria Mixed—Case Report. T. J. Billion Jr.—p. 321.

5:1-36 (Jan.) 1952

Tumors of Kidney. W. J. Baker and E. C. Graf.—p. 1.
Malignancies of Female Genital Tract. J. H. Randall.—p. 18.

Southern Medical Journal, Birmingham, Ala.

45:1-86 (Jan.) 1952. **Partial Index**

The Southern Doctor. C. Rosser.—p. 1.
Difficulties in Diagnosis of Certain Gastric Lesions. J. C. Bell.—p. 3.
Use of Protein Hydrolysates in Therapy of Peptic Ulcer. J. S. Levy. —p. 5.
Changing Pattern of Health Organization and Activities. J. W. Bass. —p. 9.
Laryngectomies in Review: 20 Years' Experience. F. E. LeJeune and M. Lynch.—p. 12.
Dextrocardia Secondary to Foreign Body in Left Bronchus: Report of Two Cases. M. Equen, F. Buckner, G. Roach and R. Brown.—p. 16.
Congenital Dysplasia of Hip Joint in Early Infancy. R. D. Hawkins. —p. 18.
Histochemical Approach to Pathology Exemplified in Studies on Glomerular Disappearance. J. F. A. McManus.—p. 24.
Extra-Mammary Paget's Disease: Discussion of Pathogenesis. J. W. Eversole.—p. 28.
Early Treatment of Thoracico-Abdominal Wounds. J. M. Mason III. —p. 30.
Continuous Spinal Anesthesia in Treatment of Severe Preeclampsia and Eclampsia. G. R. Jones, H. H. Ware Jr., E. C. Garber and P. J. McElrath.—p. 34.
Pathologic Conditions Treated by Proctologists. J. E. Linn.—p. 43.
Present Day Methods of Treatment of Carcinoma of Cervix. H. D. Kerr. —p. 47.
The Maternal Breast. D. Findley.—p. 51.
ACTH and Cortisone: Their Role in Dermatologic Therapy. J. L. Callaway.—p. 63.
Value of ACTH and Cortisone in Ocular Inflammations: Preliminary Report. G. A. Lawrence Jr.—p. 65.
Some Aspects of Negativistic Phenomena. H. P. Harris Jr.—p. 70.
*Pyloric Stenosis in Monovular Twins: Report of Case. G. C. Cunningham and J. J. Kelly.—p. 75.
*Simultaneous Herpes Zoster and Chickenpox: Report of Two Cases. S. D. Austin, W. H. Brandon and R. R. McGee.—p. 76.

Pyloric Stenosis in Monovular Twins.—A case of hypertrophic pyloric stenosis in each of monovular twins is reported, bringing the total reported cases to 12. There have been only two cases of hypertrophic pyloric stenosis reported in monovular twins with only one twin affected. The rule rather than the exception of its occurrence in both of monovular twins is strong evidence in favor of a genetic factor in the etiology.

Simultaneous Herpes Zoster and Chickenpox.—Chickenpox has frequently been noted to follow exposure to herpes. It has been postulated that the two eruptions represent different phases of the same disease. Another theory suggests that chickenpox in childhood makes the individual immune to herpes zoster in later life. Since the two diseases rarely occur simultaneously, Austin and associates present two such cases recently observed by them. One of these was a man, aged 65, who had had no known recent exposure to either chickenpox or herpes zoster and who said that he had had chickenpox as a child. His generalized varicella rash disappeared entirely in one week. The herpetic eruption on the head improved fairly rapidly after treatment was started. The second patient was a man, aged 35, who had never had chickenpox before, and there was a history of exposure to chickenpox 16 days before the onset of symptoms.

Trans. Southeastern Sec. Am. Urolog. Assn., Memphis

15th Ann. Meet.:1-142 (March) 1951. **Partial Index**

*Role of Protective Urinary Colloids in Prevention of Renal Lithiasis. A. J. Butt.—p. 1.
Management of Calculi in Lower Ureter. W. L. Champion, M. F. Fowler, R. C. Coleman Jr. and T. J. Florence.—p. 11.
Hypertension and Surgical Kidney. A. D. Puppel and E. P. Alyea.—p. 15.
Postoperative Treatment Following Prostatic Surgery. J. B. Glanton, L. M. Orr and J. C. Hayward.—p. 25.
Transurethral Resection of Prostate. E. H. Ray.—p. 29.
New Female Air Cysto-Urethroscope. D. W. Goddard.—p. 37.
Interesting Bone Changes in Plain Urograms. W. L. Fitzgerald and M. D. Thomas Jr.—p. 41.

Protective Urinary Colloids in Prevention of Renal Lithiasis.—Although both crystalloids and colloids enter into the composition of urinary calculi, most investigations concerning prevention and treatment of calculi have been directed only toward diminishing the concentration of crystalloids in the urine. From what is known of the effects of the urinary colloids in increasing the solubility of stone-forming salts, it follows that if this protective power is diminished or abolished, urinary deposits will form more readily. Butt examined urine for colloidal activity and then made efforts to increase the protective urinary colloids. The spreading properties of hyaluronidase suggested that this drug might be useful for this purpose. Urine specimens from 34 subjects were examined for degree of colloidal activity. Then 0.02 mg. of hyaluronidase dissolved in 1 cc. of isotonic sodium chloride solution was injected subcutaneously, and colloidal activity of the urine was observed at different intervals. In 28 of the 34 subjects, colloidal activity was significantly increased following injection of hyaluronidase. Colloidal activity began to rise in 10 minutes, reached a peak in from 1 to 2 hours, and remained elevated for 24 to 96 hours. The patients who showed no increase in number of colloidal particles had renal calculi. There was no sedimentation in the urine of patients who had received hyaluronidase, as is usually the case. The author concludes that a clearer understanding of the urinary colloids helps explain why hydration is important in the prevention and treatment of urinary calculi. There appears to be a correlation between the fact that the colloidal activity is elevated in the Negro race as compared to the white race, and that the incidence of stone formation is less in Negroes. Observation of elevated colloidal activity in pregnant women offers an explanation as to why pregnancy, which is so often associated with dilatation and stasis of the urinary tract and increased excretion of calcium, is not more frequently complicated by urinary calculi. The fact that patients who have renal calculi have decreased urinary colloids suggests that reduction or absence of these protective colloids are a factor in the formation of stones in these patients.

U. S. Armed Forces Med. J., Washington, D. C.

2:1779-1932 (Dec.) 1951. **Partial Index**

Blood Vessel Bank. F. N. Cooke, D. M. Kuhns, J. T. Elston and others. —p. 1779.
Treatment of Leukemia and Similar Disorders. R. H. Smith.—p. 1787.
Defensive Medical Aspects of Biologic Warfare. M. J. Hantover.—p. 1795.
The Orthopedist in Above-the-Knee Amputations. L. E. Abt and A. Stern. —p. 1801.
Adenomatoid Tumor of Epididymis. U. L. Meeter and J. W. Schwartz. —p. 1815.
Aureomycin Therapy for Ambulatory Patients. L. H. Roth.—p. 1829.
Vasa Praevia. I. A. Beychok.—p. 1833.
Self-Administration of Mercaptomerin Sodium. B. E. Pollock and J. O. Gillespie.—p. 1837.
Surgical Importance of Schoenlein-Henoch Disease. E. T. Gordon. —p. 1845.
Echinococcus Cysts of Liver with Report of Two Cases. L. G. Bell, J. L. Yon and D. J. Williams Jr.—p. 1851.
Antibiotics in Treatment of Relapsing Fever. I. B. Harrison and R. M. Whittington.—p. 1859.
Intrahepatic Calcification. S. A. Kaufman.—p. 1863.
Diagnostic Significance of Fragment Displacement in Fractures of Carpal Navicular. G. H. Chambers and J. D. Blair.—p. 1871.
Infectious Mononucleosis Manifested by Diarrhea. S. H. Walker. —p. 1875.
Thrombosis of Aorta Arising from Patent Ductus Arteriosus. M. Kurzrok, C. V. Carlson and A. T. Ooghe.—p. 1879.
Artificial Pneumothorax in Pulmonary Tuberculosis. R. E. Mardis and R. G. Cowley.—p. 1883.
Acute Porphyria with Intestinal Carcinoma. C. D. Chaput and J. J. Timmes.—p. 1899.

FOREIGN

Acta Haematologica, Basel

7:1-62 (Jan.) 1952. **Partial Index**

*Study of Metabolism of Folic Acid and of Citrovorum Factor. K. Hausmann and K. Mulli.—p. 1.
Life Span of Red Blood Corpuscles in Erythronophthisis (Including a Method for Estimating of Fecal Stercobilinogen). H. S. Baar.—p. 17.
Radioactive Arsenic in Treatment of Hodgkin's Disease and of Mycosis Fungoides. L. Mallet, G. Marchal and G. Duhamel.—p. 27.

Metabolism of Folic Acid and Citrovorum Factor.—Citrovorum factor was given a therapeutic trial in 10 patients with pernicious anemia, 2 with symptomatic megaloblastic anemia, 3 with agranulocytosis, and 2 with idiopathic aplastic anemia. Two patients with pernicious anemia were given 6 mg. of synthetic citrovorum factor daily by mouth, but did not respond, and one who was given 9 mg. daily by mouth obtained only a suboptimal hematopoietic effect. In nine patients who were given 5 to 15 mg. of synthetic citrovorum factor daily intramuscularly the erythrocyte level was restored to nearly normal and the megaloblasts in the bone marrow disappeared. One patient was given a single massive intramuscular injection of 40 mg. of citrovorum factor obtained from bovine liver without significant effect on the hematopoiesis. One of the two patients with symptomatic megaloblastic anemia did not respond to the synthetic citrovorum factor, while the number of erythrocytes was restored nearly to normal in the other. The patients with aplastic anemia and agranulocytosis did not respond to the treatment. Microbiological assays of the urine following administration of folic acid and citrovorum factor directly into the colon showed little evidence of absorption from this organ, but following oral or parenteral administration the urinary output increased significantly. Folic acid in high doses was found to inhibit the growth-promoting effect of vitamin B_{12} on L. Leichmannii; high doses of citrovorum factor, thymine and thymidine did not exert such an antagonistic effect. Studies of the gastric juice of patients with pernicious anemia revealed reduced catalase and increased peroxidase activity; by an oxidative process the citrovorum factor is transformed to folic acid or to a substance similar to folic acid, while vitamin B_{12} and vitamin C are destroyed. These results may explain the pathogenesis of neurological symptoms and the favorable effect of antibiotics on pernicious anemia.

Annals of Rheumatic Diseases, London

10:393-536 (Dec.) 1951

Histopathology of Diarthrodial Joints in Ankylosing Spondylitis. B. Cruickshank.—p. 393.
Changing Pattern of Rheumatoid Arthritis. T. R. Littler.—p. 405.
Effect of Still's Disease on Haemopoietic System. B. Schlesinger and I. A. B. Cathie.—p. 412.
Hyaluronidase Spread and Effect of Salicylates in Rheumatic Fever. D. H. Atlas, P. Gaberman and H. Eisenberg.—p. 418.
Cortisone, Allergy, and Rheumatic Fever. D. A. Long.—p. 427.
Further Observations on Use of Pregnenolone in Rheumatoid Arthritis. G. N. Myers and D. N. Ross.—p. 432.
Ultrasoundwave Treatment of Chronic Disorders of Locomotor System. A. Sonnenschein.—p. 441.
Effectiveness of Different Forms of Heating. H. M. Whyte and S. R. Reader.—p. 449.

Arquivos de Neuro-Psiquiatria, São Paulo

9:303-392 (Dec.) 1951. **Partial Index**

*Arteriovenous Angiomas of Brain. E. Moniz.—p. 303.
Chronic and Acute Epiduritis. T. Iusausti and R. F. Matera.—p. 324.
Rehabilitation in Neurosurgery. E. D. Rocca and F. A. Escardó.—p. 343.

Arteriovenous Brain Angiomas.—Moniz emphasizes the importance of cerebral angiography for the diagnosis and surgical treatment of arteriovenous angiomas of the brain and describes a new technique for the diagnosis of arteriovenous angioma of the carotid zone. It consists of the rapid passage of arterial blood containing the opaque substance into the upper longitudinal sinus through a large anastomosing vein. The parietal arteries yield the arterial blood to the anastomosing veins of the angioma. In a large number of cerebral arteriograms the author found only one such lesion, which was located in the rolandic region, diffusing itself into the parietal region. The patient complained of an acute pain in the left hip joint, which disappeared and was followed by hemiplegia that developed slowly for 48 hours. Jacksonian epilepsy and mental disturbances developed later. The symptoms, with the exception of hemiplegia, were due to disorders of circulation of the brain, with consequent transient or permanent ischemia in certain zones of the cerebral hemisphere. Hemiplegia in this case was due to a small hemorrhage from rupture of an angiomatous vessel. Fatal hemorrhage has been observed in other cases. The surgical treatment, as carried out by the author, consisted of ligation of the common carotid artery. Direct ligation of the angiomatous veins was successful in a case of angioma of the posterior temporal region that was deeply rooted in the brain tissues.

British Journal of Tuberculosis, London

46:1-80 (Jan.) 1952. **Partial Index**

Sir Robert Young. G. E. Beaumont.—p. 3.
The Place of the General Practitioner in the Tuberculosis Service. G. O. Barber.—p. 19.
Spontaneous Pneumothorax Resulting from Pneumoperitoneum Therapy. J. S. Jones and K. B. Yuill.—p. 30.
Pulmonary Adenomatosis. J. C. Valentine and N. Wynn-Williams.—p. 37.
Pneumoconiosis in Boiler Scalers. L. Dunner, M. S. Hicks and D. J. T. Bagnall.—p. 43.
Krukenberg Tumour Presenting as Pleural Effusion: Report of Case Simulating Meigs' Syndrome. P. Ellman and J. H. P. Johnson.—p. 60.

Glasgow Medical Journal

32:333-362 (Dec.) 1951

*Polycystic Disease of Kidneys and Intracranial Aneurysms. Etiology and Inter-Relationship of These Conditions: Review of Recent Literature and Report of Seven Cases in Which Both Conditions Coexisted. R. A. P. Brown.—p. 333.
Haematometra: Review of Literature with Clinical Illustrations. C. P. Douglas.—p. 349.

Polycystic Disease of Kidneys and Intracranial Aneurysms.—Polycystic disease of the kidneys and aneurysms of the intracranial arteries have both been attributed to congenital defects and their simultaneous occurrence is therefore of interest. Brown cites previous reports of the association of the two lesions and presents the history of a woman who had a subarachnoid and cerebral hemorrhage at 21 and who nine years later showed evidence of polycystic renal disease. There was no recurrence of hemorrhages despite development of hypertension. The autopsy reports of two Glasgow hospitals were then examined, and in 11,245 autopsies six cases of polycystic kidney associated with intracranial aneurysm were found. The relationship was present in 4% of cases of aneurysm and 16.6% of cases of polycystic kidney. It is concluded that polycystic kidneys and intracranial aneurysms are associated more frequently than would occur by chance. Although hypertension and vascular degeneration may play some part in the development of the aneurysms, it is more probable that there is a common etiology. Although coarctation of the aorta is more widely known as an associated finding with intracranial aneurysms, the association with polycystic disease appears to be more common.

Helvetica Medica Acta, Basel

18:559-648 (Dec.) 1951. **Partial Index**

Investigations on Renal Diabetes. F. Reubi.—p. 559.
Myocardosis in Hepatic Cirrhosis: Further Investigations. M. Oppenheim. —p. 573.
*Plasma Staining in Differential Blood Picture as Index of Dysproteinemia. H. R. Reufer and M. Schwarzenbach.—p. 578.
*Use of Nicotinic Acid in Disturbances of Cerebral Circulation, Particularly in Hemiplegia Following an Apoplectic Stroke. J. Mentha and J. Steponavicius.—p. 608.

Plasma Staining as Index of Dysproteinemia.—This paper is concerned with the staining of plasma observed in certain cases when differential blood counts are made. This phenomenon, which is designated as "film," was further investigated in 150 cases and three different intensities of film were detected. The following disorders were observed in patients whose plasma showed the staining or film: myeloma, acute and chronic leukemia, Hodgkin's disease, sarcoma, carcinoma, cirrhosis of the liver, macrocytic anemia, and chronic infections such as tuberculosis and isolated cases of reticulosis. There is considerable

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evidence that the film or increased uptake of dye by the plasma is the result of a quantitative shifting in the various protein components. The staining is more intense the more the quantitative ratio of albumin to globulin shifts toward globulin.

Nicotinic Acid in Disturbances of Cerebral Circulation.—If the vasodilating effect of nicotinic acid is to be utilized in the early stages of cerebral circulatory disturbances, the hemorrhagic should be differentiated from embolic, thrombotic, or spastic conditions. Nicotinic acid should not be used if there is hemorrhage. This paper describes the results obtained with nicotinic acid in 20 patients who had hemiplegia or hemiparesis resulting from cerebral hemorrhage, embolism, or malacia. In one, who had arteriosclerosis and a malacic focus, treatment with nicotinic acid was begun on the second day; in another patient administration of nicotinic acid was started on the sixth day after a cerebral hemorrhage. Both patients made good progress. Of the remaining 18 patients, 13 could be observed during a period in which they received the customary nursing care but no nicotinic acid, so that subsequent improvement during the administration of nicotinic acid can be ascribed to this medication. Ten of the 13 patients had a definite improvement in their active movements, whereas three showed no improvement. The other patients likewise showed improvement, which however cannot be definitely ascribed to the nicotinic acid therapy. Nicotinic acid did not prevent further apoplectic strokes, and it had no prolonged effect on the blood pressure. It caused no serious secondary effects.

Journal International de Chirurgie, Brussels

11:451-550 (No. 5 & 6) 1951

Surgical Treatment of Mitral Stenosis: Indications. E. Derra.—p. 451.
*Surgical Treatment of Massive Pulmonary Embolism. R. Benichoux. —p. 464.
Investigation of Microscopic Metastases in Parasternal Lymph Nodes in Cancer of Breast: Localization with Regard to Intercostal Spaces. E. Dahl-Iversen and B. Soerensen.—p. 492.
Management of Chronic Osteitis and Osteomyelitis with Coagulum of Autogenous Blood + Penicillin + Thrombin (On the Basis of Results in 56 Cases). L. Winter.—p. 510.
Pseudoarthrosis with Loss of Substance in Forearm: Treatment by Bone Grafts. W. Merino.—p. 525.
*Rheoangiography in Disturbance of Peripheral Circulation: Treatment and Evaluation of Efficacy. W. Kerschner and W. Mandl.—p. 536.

Trendelenburg's Operation for Massive Pulmonary Embolism. —Benichoux points out that although Trendelenburg performed the first embolectomy for massive pulmonary embolism 32 years ago, the indications for the operation are by no means clear. This study reviews 22 embolectomies performed in a Stockholm hospital from 1926 to 1949. Nine of the patients had been operated on for lesions of the digestive tract, three for gynecologic disorders, six for lesions of the limbs, three for urologic disorders, and one for hernia. Only nine of the patients had signs or symptoms that suggested that a massive pulmonary embolism might develop postoperatively. Since 1939 heparin has been employed in such cases at the Sabbatsberg Hospital, greatly reducing the morbidity and mortality rate of pulmonary embolisms. Use of heparin also helps to explain why only one of the series of 22 embolectomies has been performed since 1939. On the other hand, the deaths that have occurred since that time can be attributed to overconfidence in heparin therapy. All of the patients who died had been bedfast for long periods, but had been ambulatory for some days before the embolism occurred. Early ambulation is probably a factor in the decreasing incidence of massive pulmonary embolism. Progressive dilatation of the right heart is an important sign and is seen in every case of massive pulmonary embolism. A delay of more than 25 minutes before operative treatment may lead to a fatal outcome. The dilatation of the right heart is relieved by opening the pulmonary artery, and the embolectomy must be as complete as possible. Cardiac resuscitation and massage may be necessary, and controlled respiration with oxygen and carbon dioxide absorption is necessary until spontaneous respiration returns. Secondary pulmonary embolism after the first embolectomy is not infrequent, and some form of venous ligation may be necessary if thrombosis in the lower extremities is suspected, e. g., femoral ligation or tying the inferior vena cava. The author concludes that pulmonary embolectomy still has a place in the treatment of selected cases of pulmonary embolism and recent advances in vascular and thoracic surgery are of great assistance in such operations.

Rheoangiography in Disturbances of the Peripheral Circulation. —The method of rheoangiography described by Kerschner and Mandl measures the quantity of blood in the extremities. It is based on rheocardiography that registers changes in electrical conduction within the body. Rheoangiography registers the change in conduction that occurs when the pulse wave passes along the limbs, and in this way the blood flow can be measured. The conduction increases with the volume of blood per unit of time and falls when the local circulation begins to fail. The curves are measured in ohms or microohms. Values obtained with the aid of rheoangiography were compared with those obtained with the oscillometer and were almost the same. On the basis of 203 measurements, averages were ascertained for pathological, transitional, and normal cases. Case histories are presented to show the possibilities of rheoangiography for diagnostic purposes and for the control of standard tests. Finally the authors show how rheoangiography can be used to evaluate therapeutic results obtained with conservative treatment (injection of curare) or with surgical treatment (lumbosacral sympathectomy); special attention is given to the functional compensation that follows treatment of peripheral circulatory disturbances.

Lancet, London

1:61-112 (Jan. 12) 1952

Power and Responsibility. F. Fraser.—p. 61.
Prevention of Eclampsia and Pre-Eclampsia. R. H. J. Hamlin.—p. 64.
The Kidney of Scleroderma. H. C. Moore and H. L. Sheehan.—p. 68.
Slow-Release Medium for Adrenocorticotrophic Hormone. H. M. Bruce and A. S. Parkes.—p. 71.
Toxicity of Dihydrostreptomycin Sulphate for Auditory Nerve. C. Don and J. Gregory.—p. 72.
Regenerative Power of Liver and Its Reserve Capacity for Excreting Bile: Their Possible Significance in Surgical Treatment of Biliary Obstruction. L. Schalm, M. J. Schulte, H. R. Bax and others.—p. 75.
Accidental Spinal Injection of Xylocaine During Attempted Epidural Analgesia. D. D. C. Howat.—p. 81.
Treatment of Cardiac Arrest: Filling the Heart by Expelling Blood from Limbs. W. W. Woodward.—p. 82.

Semaine des Hôpitaux de Paris

28:39-78 (Jan. 6) 1952. **Partial Index**

"Water-Sodium-Potassium" Diabetes, Complicating Diabetes Mellitus. A. Lichtwitz, R. Parlier, D. Hioco and others.—p. 39.
*Treatment of Rheumatic Carditis with Intra-Arterial Injections of "Streptococcus Anavaccine." M. Debray, R. Wattebled, J. Bertrand and B. Malapert.—p. 51.

Treatment of Rheumatic Carditis.—Eighty-two patients with rheumatic carditis, 11 aged less than 16 and 71 aged over 16, were treated with intra-arterial injections of streptococcus anavaccine ("cardiostreptin"), i. e., a streptococcus vaccine preparation consisting of the microorganism, its lysate, and its anatoxin. The injections were made into the femoral artery distal to a tourniquet applied tightly enough to occlude the venous but not the arterial circulation. A total of 15 injections were given at intervals of three to four days up to the fifth injection, and then at intervals of five to six days. The first dose was 0.25 cc., the next two injections 0.50 cc., the fourth and fifth injection 0.75 cc. each, the next two injections 1 cc., and so on until a maximum of 2 cc. was given in one injection. The tourniquet was removed 15 minutes after the injection. The patients were placed on a light diet and two tablets of 0.5 gm. of acetylsalicylic acid were given every day on which an injection was made. Functional disturbances, dyspnea, and precordial or left interscapulovertebral pain increased occasionally between the second and fifth injection. Improvement occurred between the sixth and eighth injection, with increased diuresis and temperature restored nearly to normal. A slight temperature rise occurred frequently between the 12th and 13th injections and was followed by convalescence. Of the 11 children, 10 had severe acute carditis and 2 died in the course of the treatment. The others made a complete recovery from the acute attack of the disease for which they were admitted to the hos-

pital. No adult died during treatment. Those with predominantly inflammatory lesions were considerably benefited, while improvement was less pronounced in patients with old cicatricial lesions. Results were particularly satisfactory in patients without preceding cardiac lesions, while results were moderate in patients with badly decompensated old valvular lesions, mitral stenosis, or severe disturbances of rhythm. Three of the latter patients died three, five, and seven months, respectively, after termination of the treatment. Of 42 patients, 15 were followed for four years, 8 for three years, and 19 for two years. They were able to lead a nearly normal life without taking any cardiac tonic or antirheumatic drug, and despite valvular lesions relapses of rheumatic carditis did not occur, even though before the treatment the majority of them had frequent recurrences and remained incapacitated. According to the authors, rheumatic fever is characterized by sensitization of the arterial system. Desensitization and vaccination should be carried out on this sensitized arterial tissue itself. The intra-arterial injections of "cardiostreptin" in the authors' patients extinguished the inflammatory process of rheumatic endomyocarditis, thus preventing development of a permanent lesion. Even long-standing valvular changes of mild degree were compensated by the return of the myocardial tonicity.

Strasbourg Médical

2:667-748 (Nov.) 1951. **Partial Index**

*Advantages of Streptomycin in Gonorrhea. R. Zorn and M. Michot. —p. 667.
Sensitization Dermatitis. P. Laugier.—p. 674.
Aging of the Skin. F. Woringer.—p. 696.
Treatment of Leg Ulcers. J. Grenier.—p. 716.

Advantages of Streptomycin in Gonorrhea.—Streptomycin is preferred to penicillin in the treatment of gonorrhea because it has little or no effect on the Treponema, and the likelihood that a concomitant syphilitic infection may be aborted, only to reappear later, is thus diminished. The danger of subsequent serious illness in patients treated for gonorrhea with penicillin is great, because very small quantities given during the period of incubation of syphilis will prevent the appearance of chancre without curing the infection. The danger might be avoided by prolonged observation, but these patients, embarrassed by their condition, are usually unwilling to submit to observation. Streptomycin in a total dose of 0.5 gm. to 2 gm., given in one or two intramuscular injections on one or two days has proved effective in 95% of the authors' cases of gonorrhea. It is safe and easy to inject, and has not been followed by any harmful effects because the period of treatment is short and the doses used are moderate.

Tidsskrift for Den Norske Laegeforening, Oslo

71:753-785 (Dec. 1) 1951

*Complications in Connection with *p*-Aminosalicylic Acid (PAS) Medication in Pulmonary Tuberculosis. S. Bøyum.—p. 753.
*Side-Effects in *p*-Aminosalicylic Acid (PAS) Treatment. P. Gundersen. —p. 756.
*Hypersensitivity to *p*-Aminosalicylic Acid (PAS): Report of Case. O. Kløvstad.—p. 759.
Motion Sickness and Its Treatment. O. Gulli.—p. 762.

Complications of *p*-Aminosalicylic Acid Treatment in Pulmonary Tuberculosis.—Bøyum's study of the cases of pulmonary tuberculosis treated with *p*-aminosalicylic acid in the Ringvål Sanatorium during the past two years showed that complications, although infrequent, may be grave in certain cases, with marked danger to the patients if the agent is not withdrawn at the right time. *p*-Aminosalicylic acid may exert a toxic effect on the liver, producing injury to the parenchyma and hypoprothrombinemia, and may affect phagocytes and thrombocytes. Hematuria and proteinuria were observed in two cases. The author recommends frequent leukocyte counts and urine analyses in patients receiving *p*-aminosalicylic acid. Prothrombin tests should be done before operation and in patients with a tendency to hemoptysis if this drug is to be administered. At Ringvål administration of *p*-aminosalicylic acid is now discontinued a couple of weeks before operative treatment and vitamin K given in prophylaxis.

Side-Effects in *p*-Aminosalicylic Acid Treatment.—A variety of complications following treatment with *p*-aminosalicylic acid have been reported. As a rule they occur in the first weeks of treatment. Gundersen says that the serious complications do not occur often, although they are reported in 5% of the cases in some series. Their gravity when they do occur suggests that patients treated with this drug should be more strictly observed than they have been heretofore. Regular examinations of the urine with respect to albumin, blood, and urobilin should be made. An exanthem or seemingly spontaneous rise in temperature should be taken as a prodrome of graver side-effects, and the treatment should be interrupted. If the symptoms are reproduced following a small test dose of the acid or its sodium salt, the treatment should be terminated; in cases with severer symptoms it is advisable to refrain from such testing. When complications are suspected the prothrombin content of the blood, bleeding time, coagulation time, and capillary resistance must be determined before operative treatment. Five cases are reported.

Hypersensitivity to *p*-Aminosalicylic Acid.—An initial rise of temperature may occur in patients who show a hypersensitivity reaction during treatment with *p*-aminosalicylic acid. When this agent is indicated a test dose of 4 gm. is advised, with determination of the temperature every other hour for the next 12 hours. Desensitization may be attempted in patients who react with increased temperature. Prophylactic preoperative treatment with vitamin K is advocated for all patients who have been treated with *p*-aminosalicylic acid. In the case described a hypersensitivity reaction occurred after 33 days of treatment, with an initial rise in temperature followed by a later rise, headache, exanthem, swelling of lymph glands, enlargement of the spleen, leukocytosis, lymphocytosis, eosinophilia, jaundice, urobilinuria and bilirubinuria, and positive thymol turbidity test. Cutaneous tests with the drug were negative. On readministration of the acid a rise in temperature, eosinophilia, and increasing thymol turbidity values were seen.

Urologia, Treviso

18:401-496 (Oct. 20) 1951

Pathology and Treatment of Hypospadias in Children. P. Romualdi. —p. 404.
*Treatment of 133 Cases of Ureterolithiasis with Procaine Hydrochloride Infiltration of Renal Pedicle. A. Trevisini.—p. 430.
Nephropathy Due to Carbon Tetrachloride: Experimental Contribution. R. Salmoni.—p. 442.
*Treatment of Cancer of Prostate with Ethinyl Estradiol. L. Migliardi. —p. 447.

Procaine Infiltration of Renal Pedicle in Ureterolithiasis.—In the last three years the author treated 133 patients with ureteral lithiasis by means of infiltration of the renal pedicle with 20 cc. of a 1% solution of procaine hydrochloride. In 69 patients with slight hematuria or infection, in whom disturbances had appeared one or two days before admission, the infiltration was performed during colic, and from one to three calculi, 5 mm. in diameter, were passed within a few hours or three days. In 12 patients, in 6 of whom the disturbances had been present for weeks or years, the infiltration was performed when colic was not present. The calculi passed some hours or two days later, and pains occurred only in the hypogastrium. Procaine infiltration during colic was ineffective in eight patients, six of whom had had symptoms for years or months, and the calculi were eliminated only after two to five infiltrations were performed when colic was not present. In 10 patients with a long history of frequent colics, ureteral catheterization was carried out when two to three infiltrations proved ineffective; the calculi passed two to three days later. In 11 patients, because of the anatomic conditions of the ureteral outlet, the block was followed by surgical diathermy. In seven the calculi were eliminated, while in three additional infiltrations were required, and the calculi passed without causing colic three days after the last infiltration. In one of these patients retrograde migration of the calculus from the ureteral outlet to the renal pelvis was observed after surgical diathermy. Infiltrations were repeated, and after one month the calculus was eliminated; it was assumed that surgical diathermy had caused antiperistalsis. In four

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patients repeated infiltrations had apparently no effect in that the calculi passed spontaneously 20, 28, 32, and 40 days, respectively, after the last block. Nephrectomy or pyelotomy was performed in four patients in whom two to three infiltrations were inefficient, and ureterolithotomy was performed in the other 15 patients in whom the treatment had failed because of the large size of the calculi. Thus, procaine hydrochloride infiltration of the renal pedicle alone was successful in 67.4% of the author's cases. The chances of success of this method in ureteral lithiasis decrease when the inflammation of the urinary tract is of long duration. The action of the anesthetic is not restricted to the ganglia and the nerves of the renal pedicle, but affects the kidney, the pelvis, and also, according to the author, the distal part of the ureter.

Ethinyl Estradiol in Cancer of Prostate.—Cancer of the prostate was treated with ethinyl estradiol ("eticiclina") in 37 patients, 21 of whom had undergone prior treatment. To three of these in whom estrogens of the stilbene series had failed, three to six 0.05 mg. tablets of ethinyl estradiol were given daily, but death occurred. In the other 18 in whom the previous treatment had good influence, 1 to 2 tablets were given daily for from several months to as long as one year. The general condition of the patients remained good, and the clinical findings, including metastatic lesions in three patients, remained stationary. Of the 16 patients who had not had previous treatment, those who were treated when their condition was still good received daily three to four 0.05 mg. tablets of ethinyl estradiol. This dose was decreased to 1 or 2 tablets daily when improvement occurred. A larger dose (8 to 12 tablets daily) was given to patients with poor general condition and severe disturbances of micturition, and this was also decreased to 1 or 2 tablets daily. Improvement in the clinical findings was quick and pronounced in all the patients, in some of whom it is still present after many months and in others after more than one year. In less than 20 days spontaneous urination was restored to normal in three patients in whom systematic catheterization had been necessary. In others dysuria decreased and residual urine disappeared. Swelling of the breast occurred in the patients during treatment, but toxic manifestations and signs of intolerance to the drug were not observed, even in cases in which massive initial doses of ethinyl estradiol were given.

Wiener medizinische Wochenschrift, Vienna

102:1-28 (Jan. 5) 1952. **Partial Index**

*Prognosis of Carcinoma of Colon. H. Finsterer.—p. 1.
Corticotropin (ACTH) and Cortisone Therapy of Bronchial Asthma. G. Holler, G. Kollert and O. Weinmann.—p. 5.
Origin of Adipose Tissue and Its Significance in Urology. K. Hutter. —p. 11.

Prognosis of Colon Carcinoma.—During World War II follow-up examinations of patients operated on for carcinoma of the colon could not be performed, and during the postwar years questionnaires were not answered by many patients who were living in foreign countries. The author's statistics are therefore concerned with 173 patients with carcinoma of the colon who were operated on during the period of 1910 to 1934 and were followed up to 1939. Of these 173 patients, 133 were subjected to resection, 27 to colostomy, and 13 to enteroanastomosis. Of the 133 patients, 29 died within the first six postoperative weeks. Of the remaining 104 who were discharged from the hospital as recovered, 6 were lost to observation, 10 died from intercurrent disease within the first five postoperative years, and 25 died within three years with symptoms of liver, peritoneal, or lung metastases. The remaining 63 patients (47.3% of those subjected to resection or 60.5% of the 104 who recovered) did not have recurrences for more than 5 and up to 24 years. Among those who recovered was a patient who was reoperated for recurrence after a two stage Mikulicz resection, and several patients who had been refused radical resection by other surgeons because of their advanced age and poor general conditions. From the prognostic point of view it is emphasized that of 12 patients operated on for colloid carcinoma, 9 did not have recurrences for more than five years, even though tumors of this type were considered inoperable by other workers. Carcinoma of the colon has the most favorable prognosis of the various types of carcinoma in men, and the next most favorable after that of carcinoma of the uterus in women. Consequently radical excision should be attempted even in apparently hopeless cases. Success of surgical intervention requires close cooperation between patient, family doctor, and surgeon. The patient must call on the family doctor when the first symptoms, such as increased constipation or discharge of blood and mucus in the feces, appear. The family doctor must insist on a series of gastrointestinal roentgenograms following oral administration of barium in addition to barium enema. The surgeon must perform the most radical operation that appears feasible under local anesthesia. Spinal anesthesia with a hypobaric solution of dibucaine (nupercaine®) hydrochloride is the method of choice. One stage or three stage resection should be preferred to two stage resection, the latter being resorted to only in cases of carcinoma of the right colon, with immediate removal of the tumor and the ileum sutured to the transverse colon to establish the "double-barreled" Mikulicz colostomy, followed later by crushing of the spur. Of 84 patients subjected to left hemicolectomy in one stage from 1910 to 1947, only 9 (10.7%) died. Of 332 patients on whom intraperitoneal anastomoses were performed up to 1948, only 5 died from breakdown of the anastomosis and resulting peritonitis, and that only because of erroneous indications. In the author's experience radical surgical intervention definitely increased the rate of permanent recoveries, despite the advanced age of the patients. Of 432 patients with carcinoma of the colon subjected to radical operation up to 1947, 91 were between the ages of 70 and 79, and 23 of them died (25.3%). Eleven patients were between the ages of 80 and 86, and four of them died (36.4%).

Zentralblatt für Gynäkologie, Leipzig

73:1827-1096 (No. 24) 1951. **Partial Index**

When Does Menstruation Begin Again Following Curettage? K. Rosenkranz.—p. 1827.
Uninterrupted Progression of Pregnancy Despite Curettage. H. Hartl. —p. 1832.
*Interruption of Pregnancy by Means of Hypertonic Solutions. H. Kallenbach.—p. 1845.
Treatment of Abortion with the Aid of Chemotherapy: Five Years Experiences. R. Häntsch.—p. 1847.

Interruption of Pregnancy with Hypertonic Solutions.—Legal processes may delay interruption of pregnancy until the pregnancy is rather advanced. In order to avoid the major operation that would be necessary under these circumstances, Kallenbach resorts to the technique described by Kovács. A 25% dextrose solution is introduced into the uterus by means of a rubber catheter; this is possible without dilatation of the uterine os. The amount of solution usually is equivalent to 100 cc. for each month of pregnancy, that is, 400 cc. for the fourth month. The fluid enters between the uterine wall and the fetal membranes. The increase in uterine volume corresponds to about that which the advancing pregnancy would produce in another month. There is little danger of uterine rupture, because the excess fluid flows off. The catheter is withdrawn after an adequate amount of fluid has been introduced. It is advisable, however, to place a tampon into the posterior vaginal vault. The uterine contents are usually expelled within 24 to 48 hours, and bleeding is generally not severe. Two factors are responsible for the elicitation of the uterine contraction: (1) the mechanical stimulus from the increased intrauterine pressure, and (2) the chemico-osmotic action of the hypertonic solution, which prolongs the effect. Physiologic solution similar to Tyrode's solution did not produce an abortion. A 10% solution of gelatin was tried and with this solution, the absorption is much slower, implying a greater mechanical action that evacuates the uterine contents, usually within 24 hours. Thus the gelatin solution was even more effective than the hypertonic dextrose solution. This method of inducing an abortion largely simulates the physiologic processes of a spontaneous delivery.

BOOK REVIEWS

Clinical Laboratory Diagnosis. By Samuel A. Levinson, M.S., M.D., Ph.D., Director of Laboratories, University of Illinois Research and Educational Hospitals, Chicago, and Robert P. MacFate, Ch.E., M.S., Ph.D., Chief, Bureau of Laboratories, Department of Health, City of Chicago. Fourth edition. Cloth. $12. Pp. 1146, with 221 illustrations and 13 plates. Lea & Febiger, 600 S. Washington Sq., Philadelphia 6, 1951.

Despite the many texts available on the subject of clinical pathology, this book remains the standard text in laboratory medicine. The book has been thoroughly revised and brought up-to-date. It has 269 more pages than the previous edition. Modern methods, which have proved to be valuable, have been added. Illustrations, many in color, with representative examples of the various types of blood dyscrasias, have been included in the chapter on hematology, and the new nomenclature adopted by the American Society of Clinical Pathologists is included in this section. Recent terminology is used throughout the text. The section on bone marrow has also been rewritten. In the discussion on blood groups and the Rh factor, a review including the technique for the determination of blocking antibodies and the Coombs' test is given. In the section on bacteriology, the latest classification by Bergey is included. There is a brief but adequate discussion on mycology as it is used in the clinical laboratory and a discussion on the methods for antibiotic study, including a screening method as well as a detailed survey of antibiotics. In the chapter on pediatric procedures, new illustrations and a report of blood dyscrasias in pediatrics as well as a review of the bone marrow findings have been included. Other sections that have been revised concern new nomenclature in tropical diseases, legal medicine and toxicology, the general search for poisons and the most important poisons, blood chemical methods, and the spectrophotometer (flame photometer) in relation to electrolyte balance studies. This last section should prove of value to the clinical laboratory, because the methods have been modified, so that the same reagents are used whether the product is read in the colorimeter or in the photometer. The authors describe the methods used in the colorimetric determinations and the way these may be converted from the photometer to the colorimeter or the reverse with only slight changes in technique and with no loss of time for the preparation of the new reagents. The usual biochemical methods are described, and there is a step-by-step description of the methodology. Among the chemical determinations discussed are ascorbic acid, alkaline and acid phosphatases, electrolyte balance studies, and sodium and potassium of the blood and urine.

The authors point out in their introduction that one of the major problems confronting a revision of a text in clinical pathology is the selection of current material and methodology of practical value. The progress in experimental medicine and clinical pathology has been rapid, and there is a tendency to include in texts more than is needed. The authors have achieved their objective in discussing the most useful methods in laboratory medicine in a concise, systematic manner. In most of the sections, there is a brief review of the basic sciences of anatomy, physiology, biochemistry, and related subjects, in order to assist the reader in the orientation of the subject as well as to benefit him in the problem of correlating the normal and abnormal findings.

The book is beautifully printed, and the illustrations are profuse and helpful. There are many plates, some of which are in color, and a 45 page index. It may be unqualifiably recommended to physicians, students, and medical technologists, as a succinct and authoritative text in clinical laboratory diagnosis.

The reviews here published have been prepared by competent authorities and do not represent the opinions of any official bodies unless specifically stated.

History of Medicine in Ireland. By John Fleetwood, M.B., D.P.H. Cloth. 21s. Pp. 420, with 19 illustrations. Browne and Nolan, Limited, Richview Press, 41/42 Nassau St., Dublin, 1951.

Dr. Fleetwood, in this readable and interesting book, admits that his work is not an exhaustive account of Irish medical practice. He does, however, relate an historic narrative that traces the development of medicine in Ireland from the pre-Christian era to the present time. In discussing the Brehon Laws, which were first promulgated several hundred years before the time of Christ, he brings us from antiquity to the present day as he points out that provision was made in the Book of Aicill for a medical referee when a dispute over treatment arose between the patient and the physician. Payment to the physician was made by the aggressor in quarrels resulting in injury and was in accordance with the social class of the wounded person. The author indicates that, even in this period, some form of medical registration was practiced.

In a pleasant and interesting fashion, the author discusses the progress of Irish medicine through the years and relates the important developments in hospitals and teaching facilities. Physicians in the United States will find the final chapter, in which the author writes of the future of Irish medicine, especially interesting. He recognizes the complexity of the problem as more and more students overcrowd the medical schools and after graduation "leave the country forever—because it pays them better." The discussions of the activities of the medical education investigating committees in 1945, 1947, and 1948 and the author's comments are enlightening. Dr. Fleetwood favors a government program wherein two physicians are appointed to a district of 3,000 persons, with the patient having free choice of his physician, "even outside his district." Under this system, a physician might earn £1,626 per year. Although Ireland "can claim to as ancient a professional tradition as any other country," she will not, because of limited population, finances, and clinical material, find it easy to become a medical center. Ireland has given great men to medicine, but most of their contributions have been made in other countries. The bibliography is valuable. Those who are interested in the political problem that medicine faces in the United States will be able to appreciate the probable results of radical change in Ireland.

The Mode of Action of Anaesthetics. By T. A. B. Harris, M.B., B.S., D.A., Anæsthetist to Guy's Hospital, London. Cloth. $8. Pp. 768, with 22 illustrations. Williams & Wilkins Company, Mount Royal and Guilford Aves., Baltimore 2, 1951.

The object of this book is to reveal how anesthetics produce their characteristic action in man, since it is believed that a thorough knowledge of the mode of action of a drug ought, inevitably, to result in its intelligent use. This volume contains four sections, each section being divided into chapters. Section one deals with narcotics, section two with anesthetics, section three with the correlation of the level of anesthetic depression of the nervous system with anesthetic sleep, loss of sensation, and loss of muscle movement and tone, and section four with metabolism during anesthesia and the side actions of anesthetics. The author includes his own speculations and conclusions. An adequate bibliography at the close of each chapter makes this a valuable reference book. Apparently, this volume appeared before Brodie's report concerning the slow rate of metabolism of thiopental sodium due to its prolonged storage in fatty tissues of the body. Reference to this work would have enhanced the discussion of intravenous anesthesia. Many physicians believe that too early administration of morphine during anesthetic recovery, as recommended by the author, is an unwise procedure, particularly from the standpoint of hypoxia. The more extensive use of mask oxygen during recovery from general anesthesia has shortened

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the excitement period and materially lessened nausea and vomiting. Spinal anesthesia has more wide acceptance and success than is indicated by the author.

The chapters are adequately illustrated with numerous tables, graphs, and mathematical formulas. A complete index is included. Consideration of the material discussed by this author makes obvious the wide knowledge a physician should have in order to provide safe anesthetic care. Anesthesiologists, research workers, and other physicians concerned with the effects of anesthetic drugs will greatly benefit from this book.

Primer for Pregnancy: An Informal and Practical Guide for the Expectant Mother. By Eve Stanton Featheringill. With foreword by Louis Langman, M.D., Assistant Clinical Professor of Obstetrics and Gynecology, New York University College of Medicine, New York. Cloth, $2.95. Pp. 241, with illustrations. Simon & Schuster, Inc., 1230 Sixth Ave., New York 20, 1951.

During the last few years many books concerning childbirth have been written by both physicians and lay persons. The author of this book is not a physician, but she is the mother of three children. She has acquired a considerable amount of knowledge concerning the psychological, emotional, and practical aspects of maternity. The book contains good advice, but the reviewer disagrees with sections of it; for example, the advice, "In a city, look in the classified telephone directory" for an obstetrician is not good.

The author is in favor of women being conscious during birth. Her first child was born while she was under an anesthetic, but not the second and third; she would not "trade the joy of the second and third for the oblivion of the first"; however, she believes that the use of final anesthesia is justified and often essential. Much time and effort has gone into this book. Whereas the author has really enjoyed her last two labors, perhaps by sheer will power, she will have a hard time convincing most of her readers that they will do the same. Nevertheless, the efforts of the author are to be commended, because any propaganda that will lead to a reduction of the present day excessive use of obstetric analgesia and anesthesia is definitely worth while. Many pregnant women will find this book useful and entertaining.

Gynaecological Endocrinology for the Practitioner. By P. M. F. Bishop, D.M. Second edition. Cloth. $3. Pp. 132, with 17 illustrations. Williams & Wilkins Company, Mount Royal and Guilford Aves., Baltimore 2, 1951.

Dr. Bishop's volume is an excellent, compact discussion of the commonest problems in endocrine gynecology. It is well written and contains much information. One of the admirable features is the fact that this is not a formal discussion, but it reflects the author's own experiences with patients and the application of sound scientific principles in this regard. The information is, therefore, most useful for the physician. There is an appendix with valuable suggestions on fertility case records, temperature charts during the menstrual cycle, tables of potency of estrogen, and therapeutic schedules. A minor criticism is that the excellent chapter on steroid chemistry is too extensive for this condensed volume. The space might be better used with other data. Otherwise, this volume can be recommended to the general practitioner and the gynecologist who wants a good basis for the study and treatment of the endocrine aspects of gynecology.

Yellow Fever in Galveston, Republic of Texas, 1839: An Account of the Great Epidemic. By Ashbel Smith, M.D., A.M. [Published by Hamilton Stuart, Galveston; Cruger & Moore, Houston; J. W. Cruger, Austin, 1839.] Together with A Biographical Sketch by Chauncey D. Leake, and Stories of the Men Who Conquered Yellow Fever. Cloth. $2.50. Pp. 135, with 3 illustrations. University of Texas Press, Austin 12, 1951.

In renaming its original structure in honor of Dr. Ashbel Smith, the University of Texas Medical Branch at Galveston provided the opportunity to reprint Dr. Smith's account of a yellow fever epidemic that occurred in Galveston in 1839. Dr. Smith, then a famous citizen of the Texas republic, obtained his B.A. and M.D. degrees from Yale University. When he received his B.A., the president of Yale said he was the best student of Latin and Greek that Yale had ever had. After Dr. Smith did graduate work in Paris, he began practicing medicine in the North Carolina hills. When a call came for volunteers to defend the Texas settlers, he made the long and rough journey to Texas, having been inspired by his friendship with the great Texas leader Sam Houston. He immediately undertook the care of the wounded and before long was appointed surgeon general of the Republic of Texas, later becoming secretary of state and the first minister of that republic to England and France. Following the admission of Texas to the Union, Dr. Smith was elected to the Texas legislature. Although opposed to secession, he raised the second Texas infantry and was its colonel. He remained active in medical affairs and took a leading part in fighting the Galveston epidemic in 1839, keeping records of cases and performing a surprising number of postmortem examinations. His clinical observations have been significantly improved on since then in only two ways: (1) by the recognition of mosquitoes as the transmitters of the infectious material and (2) by the recognition that yellow fever is caused by a virus.

This book is more than a reprint of Ashbel Smith's account of the Galveston epidemic. The editor, Chauncey D. Leake, includes the biographic sketch of Dr. Smith that was published in the *Yale Journal of Biology and Medicine* in January, 1948, and a series of articles edited by the late Josiah C. Trent that were published in 1946 in the *North Carolina Medical Journal*. These articles provide an excellent history of yellow fever and a discussion of the persons foremost in the battle to overcome its devastating effects.

Liver Disease. Consulting editor: Sheila Sherlock, M.D., F.R.C.P. Editor for Ciba Foundation: G. E. W. Wolstenholme, O.B.E., M.A., M.B. Ciba Foundation Symposium. Cloth. $4.50. Pp. 249, with illustrations. Blakiston Company (division of Doubleday & Company, Inc.), 1012 Walnut St., Philadelphia 5, 1951.

This book consists of a series of papers discussed at the International Conference on Liver Disease held in London and sponsored by the Ciba Foundation, in 1950. The subject of the conference was "Etiology of Chronic Liver Disease." Papers are divided into the following categories: protein metabolism in liver disease, etiology of hepatic cirrhosis, etiology of portal hypertension and ascites and its treatment, pigment metabolism, splenic blood flow, and infectious aspects of liver disease. Many of the papers are informal in character and involve work still in progress. The remarks of the various contributors are included verbatim. Tables, graphs, and photomicrographs are abundant.

The conference was attended and papers read by active investigators in the field from all over the world. The papers are stimulating and thought provoking and contain a great deal of unpublished material. This book should be read by all investigators interested in liver disease. Proper appreciation of this material, however, requires an extensive knowledge of the literature and of the technical procedures involved in studying liver disease. In addition, much of the material is presented in a fragmentary, unconnected fashion. Nevertheless, although this book is of interest chiefly to specialists, it is well organized and a real contribution.

Roentgen Anatomy: Roentgen anatomia. By David Steel, M.D. Cloth, $8. Pp. 109, with 108 illustrations. Charles C Thomas, Publisher, 301-327 E. Lawrence Ave., Springfield, Ill.; Blackwell Scientific Publications, Ltd., 49 Broad St., Oxford, England; Ryerson Press, 299 Queen St., W., Toronto 2B, 1951.

This neat, thin book contains 54 reproductions of roentgen films of the different parts of the human body in the usual standard positions. Opposite each roentgen reproduction is a line diagram of the same size, with every anatomic detail numbered, and, on the same page, the numbered part is identified in a listing. There is both an English and Spanish listing throughout the book. The cuts, printing, paper, and arrangement are characteristic of the meticulous artistry of the publisher. To review an anatomy book is like trying to review a dictionary; both are so factual that one often finds nothing to challenge. In the adult, human osseous anatomy is static in outline and detail if not altered by injury, disease, or age. The author, who is well known to American radiologists, is to be congratulated for providing, with simplicity, the primary facts of the interpretation of normal osseous shadows on roentgen films.

QUERIES AND MINOR NOTES

USE OF CORTISONE IN AMBULATORY PATIENTS

To the Editor:—*I practice in a poor district in which patients cannot afford expensive laboratory examinations, and they receive only a minimum of good medical care. Can cortisone be used safely and advantageously by ambulatory patients, and in what dosage and conditions?* *M.D., New York.*

Answer.—Cortisone may be administered with relative safety to ambulatory patients having most conditions for which cortisone is known to be useful, provided that the physician maintains proper supervision of the patients. The smallest effective dose should be used. No specific statement can be made regarding the size of doses, since this varies with the nature and acuteness of the disease and with the age and sex of the patient.

Prior to administration of cortisone, a thorough medical history, physical examination, roentgenogram of the thorax, urinalysis, leukocyte count, hemoglobin determination, and serologic test for syphilis should be performed. Other procedures may be indicated in special cases. During administration of cortisone, the physician should examine the patient periodically, with special regard for detection of undesired physiological effects. Initially, and whenever doses greater than 100 mg. are employed daily, such examinations are usually required every one to three or four days; later, examinations may be necessary only every one to two weeks, if daily doses of 75 to 100 mg. are used, or every two to six weeks, if daily doses less than 75 mg. are employed.

Laboratory tests are usually less important than clinical observation of the patient, in respect to proper regulation of dosage of cortisone. Urinalysis should be performed at intervals varying from one week to two or three months, depending largely upon the dose of cortisone administered. Hemoglobin and leukocyte determinations are required less frequently than urinalyses. Determination of blood electrolytes is usually unnecessary as a routine procedure, unless daily doses greater than 100 mg. are employed. Other laboratory examinations may be required by special circumstances.

The main contraindications to ambulatory therapy with cortisone are: 1. Illnesses that require rest in bed as part of the general program of treatment; for example, acute rheumatic fever. 2. Illnesses that by their critical nature require the close medical and nursing supervision that can be achieved only in the hospital. Crises of acute lupus erythematosus or acute adrenal insufficiency exemplify this category. 3. The presence of complicating conditions that increase the risk of administration of cortisone to such an extent that supervision in the hospital would be required for the patient's safety. The risk of administration of cortisone is increased in patients with psychosis or severe psychoneurosis, cardiovascular or renal insufficiency, diabetes mellitus, osteoporosis, peptic ulcer, pregnancy, convulsive disorders, and various infections. Even in the presence of some of these complications, hospitalization may be unnecessary. The risk of administration of cortisone must be evaluated individually for each patient.

ALCOHOLIC INTOXICATION

To the Editor:—*Is a male automobile driver who has consumed five alcoholic drinks during three hours capable of driving an automobile? Would this amount of liquor intoxicate this man?* *M.D., Illinois.*

Answer.—The degree of intoxication does not depend on the amount of alcohol that a person consumes but on the amount of alcohol that his body fails to oxidize or eliminate. In other words, it is the unburned alcohol in the body that causes intoxication. The average 150 lb. (68 kg.) man oxidizes and eliminates about 7 to 10 cc. of absolute alcohol per hour. If he would space his drinks, he could drink a pint of 100 proof liquor in 24 hours without showing physical or chemical signs of intoxication. The answer to the query is made difficult by the fact that absorption of alcohol is delayed by the presence of food in the stomach and that the dilution of the alcohol in the stomach is also a factor. Assuming that the query refers to a 150 lb. man of average build, and that each drink contains ½ oz. (15 cc.) of absolute alcohol, he would have consumed 2½ oz. (75 cc.) of alcohol. This amount could cause a maximal blood alcohol of about 0.12% by weight, if no oxidation took place; however, in the three hours of drinking he would oxidize about 1 oz. of alcohol, thus reducing the blood alcohol to a maximum of about 0.08%. From the standards set by the Committee on the Study of Motor Vehicle Accidents of the American Medical Association and the Committee on Tests for Intoxication of the National Safety Council, this would be interpreted as an amount that is usually associated with some loss of that clearness of intellect and self-control that he would ordinarily possess, but the obvious physical symptoms of the person should be taken into consideration before a diagnosis of intoxication is made. The unfortunate part of the calculations based on the amount consumed is that they can show a possible maximum blood alcohol, but the actual amount is usually unpredictably below this figure. The only reliable way to determine this man's state of intoxication would be to test the per cent of alcohol in his blood, breath, or urine.

ETHYLENE AND CYCLOPROPANE ANESTHESIA

To the Editor:—*What are the distinctive characteristics of ethylene and cyclopropane anesthesia?*

William E. Howes, M.D., Great Neck, N. Y.

Answer.—Cyclopropane and ethylene are similar in some ways but distinctly different in others. Both are gases and are obtained compressed in metal cylinders. However, the cylinders differ considerably; ethylene is packaged under much greater pressure and comes in heavy steel cylinders, while cyclopropane is packaged under low pressure and can be obtained in light steel cylinders. Ethylene has a rather strong characteristic odor, whereas cyclopropane has much less odor. The quantity of ethylene used usually is much greater than that of cyclopropane; the difference in odor is more noticeable partly for that reason. Both are inflammable and explosive when mixed with air or oxygen. With either gas one must use all precautionary measures, especially the Horton intercoupler. The boiling point of ethylene is −103.9 C (−155 F) and of cyclopropane −34.4 C (−30 F). The ignition temperature of ethylene is 543 C (1009 F) and of cyclopropane 498.9 C (930 F). The explosive limits of these gases are as follows: per cent in air, for ethylene, 2.75 in the lower limit and 28.6 in the upper, and for cyclopropane, 2.41 in the lower limit and 10.3 in the upper; per cent in oxygen, for ethylene, 3.1 in the lower limit and 79.9 in the upper, and for cyclopropane, 2.45 in the lower limit and 63.1 in the upper; per cent in nitrous oxide, for cyclopropane, 3.0 in the lower limit and 28.0 in the upper limit. The gas vapor density (when air = 1) for ethylene is 0.97 and for cyclopropane, 1.46.

Both gases must be used carefully to avoid the possibility of ignition by flame, cauterizing agent, or static electricity. Ethylene is administered with a gas machine. The continuous flow method or the carbon dioxide absorption technique may be used. Cyclopropane, being an expensive gas, is almost always given by the soda lime absorption technique. Cyclopropane with oxygen produces much more relaxation in anesthetic doses than does ethylene with oxygen. Use of cyclopropane usually is avoided in patients with cardiac disease, whereas ethylene is the anesthetic of choice in such patients. Ethylene is usually given in an 80% concentration with 20% oxygen, a mixture that tends to put it out of the explosive range. Cyclopropane is given

The answers here published have been prepared by competent authorities. They do not, however, represent the opinions of any official bodies unless specifically stated in the reply. Anonymous communications and queries on postal cards cannot be answered. Every letter must contain the writer's name and address, but these will be omitted on request.

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in low concentrations with a high percentage of oxygen; such a mixture does not put cyclopropane out of the explosive range nor does a similar mixture with nitrous oxide.

Each of these gases is administered advantageously with some diethyl ether, and each is complemented advantageously by the use of curare for producing relaxation. In goiter operations on patients with a high metabolic rate, adverse effects during emergence from ethylene anesthesia were observed in the days before Lugol's solution and more recent remedies were used in the preoperative preparation of these patients. The essential difficulty was that these patients required more oxygen than they received when given deep ethylene anesthesia. Cyclopropane has been used with better results in goiter cases because of the large amount of oxygen present in the inhaled mixture. However, patients with goiter often have cardiac difficulties, and for this reason cyclopropane is not generally considered indicated for this type of operation. For ordinary operations, such as laparotomy, cyclopropane has been used extensively, but occasionally when ether has not been used with it, the patient has shown alarming symptoms of cardiovascular collapse when anesthesia was discontinued. This reaction is called cyclopropane shock, or carbon dioxide absorption technique shock. It is controversial as to what mechanism is involved in bringing about this condition. It seems to be definitely associated with the technique of administering cyclopropane and oxygen without nitrous oxide and ether induction, and with administration of nitrous oxide and oxygen at termination of anesthesia. Patients go to sleep more quickly with cyclopropane than with ethylene, and they often awake more quickly from cyclopropane. In the postoperative period, there is usually little nausea or vomiting caused by either agent. The present day agents and methods of anesthesia permit one to utilize methods that are fireproof and explosion proof, that make it pleasant for the patient to be anesthetized, and that leave emergence from anesthesia free from nausea or vomiting. Ethylene and cyclopropane are being replaced more and more by these new agents.

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CATARACTS AND DIATHERMY

To the Editor:—*I have seen reports of lenticular opacities secondary to Raytheon Microtherm irradiation on animals. The authors suggest there may be some tendency for the formation of cataracts from this type of treatment around the orbit. I would appreciate your opinion as to whether the use of deep heat (Microtherm) is dangerous when used around the orbit. Is there any type of shield that could be used over the eyes to protect the orbit from this heat and damage?*

M.D., Arkansas.

Answer.—There is a possibility of damage to living tissue due to excessive heating by diathermy. In the case of heating by microwave diathermy, there is special susceptibility of ischemic tissue, areas containing large amounts of fluid, and tissues overlying bony prominences to excessive doses. Lenticular opacities have been produced in experimental animals whose eyes were exposed to microwave diathermy.

From the experimental evidence available, it would seem possible that eyes subjected to excessive dosage may develop cataracts. One method of minimizing this danger is that of placing a metal cone over the eye to reflect the microwaves. A description of such a device is to be found in the paper entitled "Heating of the Human Maxillary Sinus by Microwaves" by Stafford L. Osborne and John J. Ballenger (*Brit. J. Phys. Med.* **13**:177-180 [Aug.] 1950).

ANTABUSE® AND GENERAL ANESTHESIA

To the Editor:—*Would anesthesia be contraindicated for a patient who is taking antabuse®? How will such a patient respond to anesthesia?*

T. F. Brinton, M.D., Eugene, Ore.

Answer.—Patients taking tetraethylthiuramdisulfide (antabuse®) are not good candidates for anesthetization with any general anesthetic agent, because the drug interferes with utilization of oxygen by nervous tissues and because cardiac vascular complications might occur unless the administration of tetraethylthiuramdisulfide has been discontinued for some days before the anesthetic is administered. The administration of ether would be somewhat similar to the administration of alcohol to patients who are being given tetraethylthiuramdisulfide, since much acetaldehyde is formed, and this is the cause of the reaction. Paraldehyde, a polymer of acetaldehyde, must be avoided, since it causes a positive reaction to tests for acetaldehyde.

If a general anesthetic is administered, whether it be thiopental (pentothal®) sodium, curare, or cyclopropane, a high percentage of oxygen must be administered simultaneously. A great fall in blood pressure may be treated by the parenteral administration of fluids, particularly a 6% solution of "dextran" (6% dilution of polydispersoid glucose polymer) in an isotonic sodium chloride solution, a 3.5% solution of polyvinyl pyrrolidone in Tyrode's solution, and perhaps by the administration of a vasopressor agent. Unless the operation is an emergency, it would be better to prepare the patient for operation by discontinuing the administration of tetraethylthiuramdisulfide for several days.

DYSPNEA AND CHOKING SENSATIONS

To the Editor:—*A 33-year-old white man complains of dyspnea and a choking sensation in his throat. His electrocardiogram shows normal results, except for a slow pulse rate of 56. After exercise, his heart rate increases to 100 beats per minute but returns to normal in three minutes. His blood pressure is normal. His basal metabolism was +32 in one test, and, five days later, on another test it was +29. The protein bound iodine level was 5.5 ug. A roentgenogram of the chest shows normal results. His nose was operated on twice at the veterans hospital, with 100% improvement. Coffee and cigarettes cause mental confusion. The patient had three or four drinks recently and had an attack of tachycardia with shortness of breath. Is it possible that he has hyperthyroidism? Is the determination of the protein bound iodine level always as accurate as it should be? If this is not hyperthyroidism what factors would be responsible for this condition?*

A. L. Henrichsen, M.D., Van Nuys, Calif.

Answer.—A basal metabolism is a measurement of oxygen consumption and can be elevated by a number of conditions. Moreover, any laboratory error, such as a leak in the machine or the failure of the patient to be in basal condition, tends to raise the metabolism. Protein bound iodine levels may be abnormally high in the absence of hyperthyroidism when a patient has been taking iodine. Moreover, this test is difficult to perform, and final conclusions should not be drawn from a single test. In the complete absence of tachycardia or clinical evidence of hyperthyroidism, and, in the absence of goiter, one would be reluctant to make a diagnosis of hyperthyroidism. Moreover, the dyspnea and choking sensations are not characteristic of hyperthyroidism but are more often associated with functional states. It would not be surprising if this patient's disease were functional in origin.

CHRONIC ECZEMA IN A HOUSEWIFE

To the Editor:—*For two years I have been treating a 35-year-old woman for eczema of the hands and forearms. I have advised her to avoid the use of various soaps and washing powders, have prescribed several types of ointments, and have given the patient weekly injections of histamine in gradually increasing dosages. Could you advise me as to another type of treatment? The eczema had cleared up, and for no apparent reason it has flared up again, with deep cracks in the skin and severe irritation. I would like an opinion concerning the value of ethylene disulphonate in the above case.*

B. C. Kappmeyer, M.D., Hamilton, Ill.

Answer.—Ethylene disulphonate for the treatment of allergic diseases had a short vogue some years ago but passed into oblivion. It is difficult to advise regarding a case of chronic eczema of the hands in a woman doing housework. She may have simple irritant dermatitis from contact with substances too strong for her skin or from things to which her skin is hyper-

sensitive. She may have nummular eczema that has been irritated, a so-called infectious eczematoid dermatitis, the id type of eczematoid ringworm, or eczematous psoriasis. A diagnosis should be established. In the meantime, the treatment should consist of soothing and protective measures, such as avoiding the use of possible irritating substances, wearing gloves for housework, and applying boric acid wet dressings when the dermatitis is acute and a borated cream or mild hand lotion when the acute phase has subsided.

DIABETES MELLITUS AND CORONARY DISEASE

To the Editor:—*A man, aged 70, after having attacks of angina for several years, had a small infarction in January, 1950. His recovery was uneventful, but, resuming his usual activities, he again felt substernal pain on exertion, which was relieved by rest or glyceryl trinitrate (nitroglycerine). In October, 1950, he was informed that he had sugar in his urine and that his blood sugar (fasting level) was 235 mg. per 100 cc. With dietary management alone, his blood sugar remained below 120 mg. per 100 cc. until November, 1951, when it rose to 154 mg. per 100 cc. He was advised to take insulin. Is this necessary, in view of his history and the apparent mild to moderate diabetes?*

M.D., West Virginia.

Answer.—In a diabetic patient with coronary heart disease, hypoglycemia should be avoided; however, satisfactory control of the diabetic condition should be brought about. Glycosuria should be minimal or absent, and the venous blood sugar should be kept in the general range of 130 to 140 mg. per 100 cc. in the fasting state and not over 200 mg. per 100 cc. after taking food. If this can be achieved by a diet, which, though restricted in carbohydrate and calories, allows for an adequate protein, mineral, vitamin, and caloric intake, then insulin need not be given; however, if this cannot be attained, insulin, in appropriate doses, should be prescribed, with care taken to prevent overdosage. For the patient in question, it is likely that 8 to 12 units of NPH insulin daily, before breakfast, would suffice. The diet should provide 150 to 200 gm. of carbohydrate daily and 1.0 gm. of protein per kilogram of body weight. The amount of fat should be kept low enough to avoid overnutrition.

ABDOMINAL PAIN AFTER AN APPENDECTOMY

To the Editor:—*A man, 37 years of age, strong and accustomed to strenuous work, underwent an appendectomy in 1946. He returned home from the hospital in a week but within a month began to have general abdominal pain, which was thought to be caused by postoperative adhesions. The pain became so intense, that he entered a hospital in February of this year. An operation was performed, and the adhesions around the site of the appendix were freed. Nothing abnormal was found. For a month he was free from pain; then the pain returned and is as intense as before. Has anything been discovered recently for the treatment of adhesions?*

John A. Ferguson, M.D., Wyckoff, N. J.

Answer.—It is possible that this patient originally had a regional ileitis. This nonspecific inflammatory disease of the ileum, usually in the terminal part, frequently results in attacks of right lower quadrant abdominal pain, sometimes without diarrhea. It is usual for such patients to have had an original diagnosis of acute appendicitis, resulting in removal of the appendix. Severe inflammatory reaction of the ileum with many adhesions is a common finding in such cases, and a number of adhesions apparent at a second operation would fit in with this diagnosis. It would be interesting to have an upper gastrointestinal roentgenogram and barium enema studies done on this patient to see what can be found in the gastrointestinal tract. It would be of interest to know the patient's general condition, his weight increase or decrease, the number of daily stools, and his health between attacks.

Occasionally, an exceedingly mobile cecum can cause recurrent attacks of right lower quadrant pain, probably at the time of a partial volvulus of such a structure.

HYPERTROPHIED BREASTS

To the Editor:—*Two years ago, a woman underwent a mastoplasty for hypertrophied breasts. Previously, she had two children, and with each pregnancy her breasts had become greatly enlarged, with little regression in size following delivery. She is pregnant again (two months), and enlargement of the breasts, accompanied by much pain, is again occurring. Can something be done to reduce the stimulation of the mammary tissue? Is androgen or estrogen therapy indicated, as in the treatment of painful breast engorgement occurring in the puerperium?*

M.D., Washington, D. C.

Answer.—The increase in the size of the breasts, with associated engorgement and pain, which occurs during pregnancy, is refractory to hormonal therapy. The only treatment suggested for the patient described is proper support for the breasts. After the third or fourth month of pregnancy, there will be little increase in their size. Therefore, if this period is uneventful as concerns damaging the effects of the mastoplasty, the patient may be reassured that no further complications will develop.

PARALYSIS FOLLOWING CEREBRAL THROMBOSIS

To the Editor:—*In* The Journal (147:1507 [Dec. 8] 1951) *Dr. Francesco Tansella of Bari, Italy, inquires about rehabilitation of the hemiplegic. The answer to this inquiry states that the only form of treatment of this condition is manipulation and massage. No definite program is outlined, and the answer ends by stating that it is questionable how much can be gained by instituting treatment a year after onset.*

We have reviewed 134 cases of hemiplegia treated at the Physical Medicine and Rehabilitation Service at Bellevue Hospital; the average age of the patient was 63 years. In this series, we were able to teach 93% of the patients the activities of daily living and ambulation, and one-third were able to return to some type of gainful work, although, in some instances, the hemiplegia had existed for more than a decade. I am enclosing a monograph from the Department of Physical Medicine and Rehabilitation, outlining the detailed management of the hemiplegic patient. I am taking the liberty of sending one of these directly to Dr. Tansella.

Howard A. Rusk, M.D., Department of Physical Medicine and Rehabilitation
New York University-Bellevue Medical Center
477 First Ave., New York 16.

TESTS FOR CORONARY INSUFFICIENCY

To the Editor:—*In the Jan. 5, 1952* Journal, *in Queries and Minor Notes, a letter from Dr. Joseph Weinstein of Brooklyn states, "The frequency of false negative reactions, as well as the dangers involved in the use of the Levy anoxemia and exercise tests, has prompted the consideration of other tests." I infer that this statement applies to the Master test as well as the Levy test in the paragraph preceding the one just quoted. Physicians who use the Master "2-step" exercise test are disturbed by the repetition of the assertion that the test is dangerous. Not only is there no justification for this, but it is an allegation that I feel is used merely as an excuse for recommending another test in which the writer is interested.*

In thousands of tests personally observed by my co-workers and me in the office and clinic, there has never been a single untoward accident. Occasionally, perhaps, by pure coincidence, some patient may have an attack of acute coronary disease while walking on the two steps; however, there is no danger if the proper precautions are observed, i. e., performing the test only when the 12 lead control electrocardiogram is normal, always performing the single "2-step" before a double test is performed, and, finally, stopping the test if pain appears.

Simon Dack, M.D.
122 East 78th St., New York 21.

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